Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1626GMS

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS	4	OCT 28	KOREAPAT now available on STN
NEWS	5	NOV 30	PHAR reloaded with additional data
NEWS	6	DEC 01	LISA now available on STN
NEWS	7	DEC 09	12 databases to be removed from STN on December 31, 2004
NEWS	8	DEC 15	MEDLINE update schedule for December 2004
NEWS	9	DEC 17	ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	10	DEC 17	COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	11	DEC 17	SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	12	DEC 17	CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	13	DEC 17	THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
NEWS	14	DEC 30	EPFULL: New patent full text database to be available on STN
NEWS	15	DEC 30	CAPLUS - PATENT COVERAGE EXPANDED
NEWS	16	JAN 03	No connect-hour charges in EPFULL during January and February 2005
NEWS	17	JAN 11	CA/CAPLUS - Expanded patent coverage to include Russia (Federal Institute of Industrial Property)

NEWS EXPRESS	JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:51:10 ON 25 JAN 2005

=>
Uploading
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Do you want to switch to the Registry File?
Choice (Y/n):
Switching to the Registry File...
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 10:51:25 ON 25 JAN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 23 JAN 2005 HIGHEST RN 819046-01-0
DICTIONARY FILE UPDATES: 23 JAN 2005 HIGHEST RN 819046-01-0

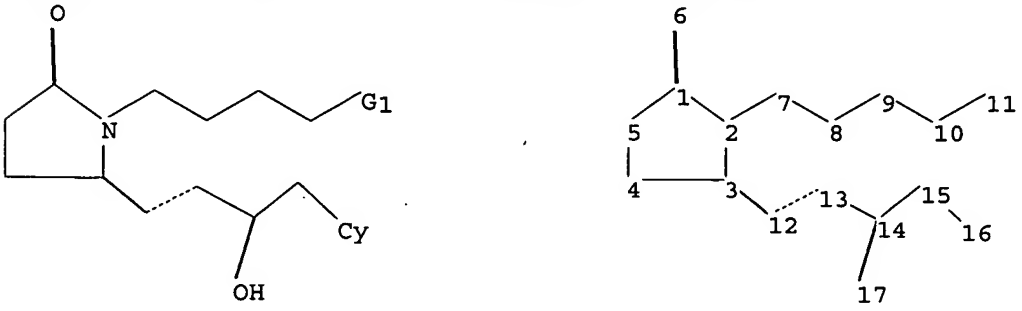
TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10668633.str



chain nodes :
6 7 8 9 10 11 12 13 14 15 16 17

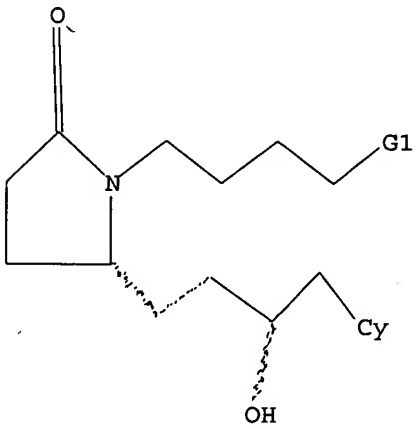
ring nodes :
1 2 3 4 5
chain bonds :
1-6 2-7 3-12 7-8 8-9 9-10 10-11 12-13 13-14 14-15 14-17 15-16
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-6 2-3 2-7 10-11 12-13 14-17 15-16
exact bonds :
1-5 3-4 3-12 4-5 7-8 8-9 9-10 13-14 14-15
isolated ring systems :
containing 1 :

G1:COOH,Hy

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:Atom 17:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 COOH,Hy

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 10:51:43 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 91 TO ITERATE

100.0% PROCESSED 91 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS: 1248 TO 2392
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 10:51:50 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1767 TO ITERATE

100.0% PROCESSED 1767 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

L3 2 SEA SSS FUL L1

=> FIL CAPLUS

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	161.33	161.54

FILE 'CAPLUS' ENTERED AT 10:51:55 ON 25 JAN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 25 Jan 2005 VOL 142 ISS 5
FILE LAST UPDATED: 24 Jan 2005 (20050124/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 1 L3

=> d l4 ibib abs hitstr tot

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2003:991395 CAPLUS
DOCUMENT NUMBER:	140:23287
TITLE:	2-Pyrrolidinone derivatives for use as EP4 receptor agonists in the treatment of eye diseases such as glaucoma
INVENTOR(S):	Billot, Xavier; Young, Robert N.; Han, Yongxin
PATENT ASSIGNEE(S):	Merck Frosst Canada & Co., Can.
SOURCE:	PCT Int. Appl., 65 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003103772	A1	20031218	WO 2003-CA838	20030602

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-386499P P 20020606
US 2003-460134P P 20030403

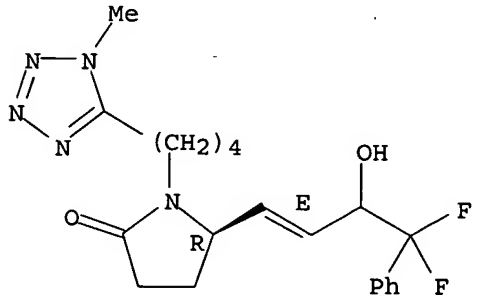
OTHER SOURCE(S): MARPAT 140:23287

AB This invention relates to 1,5-disubstituted 2-pyrrolidinone derivs. as potent selective agonists of the EP4 subtype of prostaglandin E2 receptors, topical formulations containing the same, and their use in the treatment of glaucoma and other conditions which are related to elevated intraocular pressure in the eye of the patient.

IT **634193-15-0P 634193-43-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ophthalmic compns. containing pyrrolidinone derivs. as EP4 receptor agonists for treatment of eye diseases)

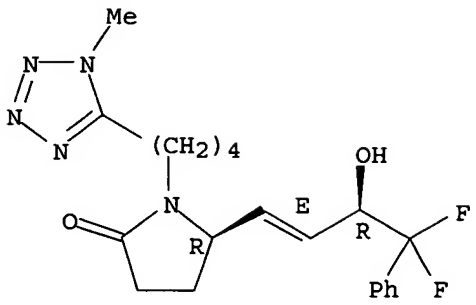
RN 634193-15-0 CAPLUS
CN 2-Pyrrolidinone, 5-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-1-[4-(1-methyl-1H-tetrazol-5-yl)butyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 634193-43-4 CAPLUS
CN 2-Pyrrolidinone, 5-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-1-[4-(1-methyl-1H-tetrazol-5-yl)butyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	8.54	170.08

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.73	-0.73

FILE 'REGISTRY' ENTERED AT 10:56:33 ON 25 JAN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 23 JAN 2005 HIGHEST RN 819046-01-0
DICTIONARY FILE UPDATES: 23 JAN 2005 HIGHEST RN 819046-01-0

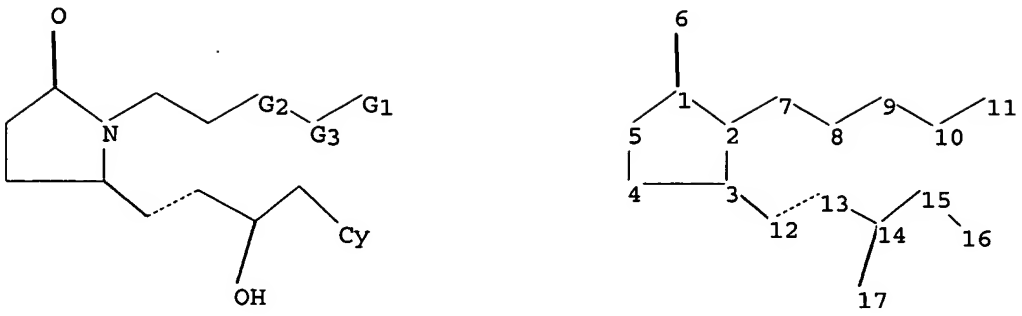
TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10668633a.str



chain nodes :
6 7 8 9 10 11 12 13 14 15 16 17
ring nodes :
1 2 3 4 5
chain bonds :
1-6 2-7 3-12 7-8 8-9 9-10 10-11 12-13 13-14 14-15 14-17 15-16
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-6 2-3 2-7 8-9 9-10 10-11 12-13 14-17 15-16
exact bonds :
1-5 3-4 3-12 4-5 7-8 13-14 14-15
isolated ring systems :
containing 1 :

G1:COOH,Hy

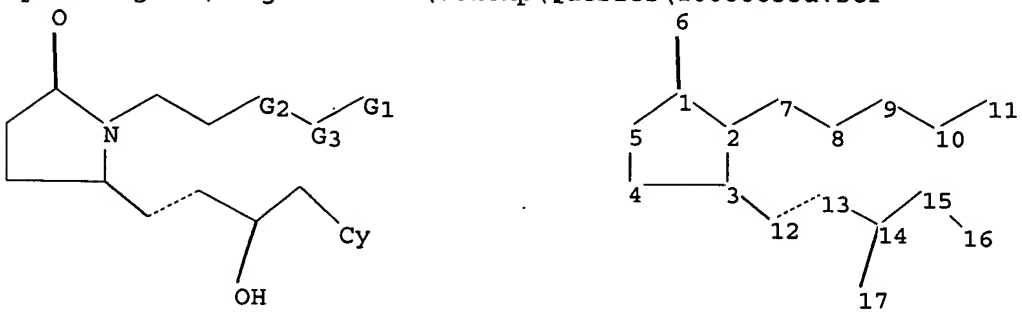
G2:O,CH2

G3:Ph,CH2,Hy,Ak

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:Atom 17:CLASS

L5 STRUCTURE UPLOADED

=>
Uploading C:\Program Files\Stnexp\Queries\10668633a.str



chain nodes :
6 7 8 9 10 11 12 13 14 15 16 17

ring nodes :
1 2 3 4 5
chain bonds :
1-6 2-7 3-12 7-8 8-9 9-10 10-11 12-13 13-14 14-15 14-17 15-16
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-6 2-3 2-7 8-9 9-10 10-11 12-13 14-17 15-16
exact bonds :
1-5 3-4 3-12 4-5 7-8 13-14 14-15
isolated ring systems :
containing 1 :

G1:COOH,Hy

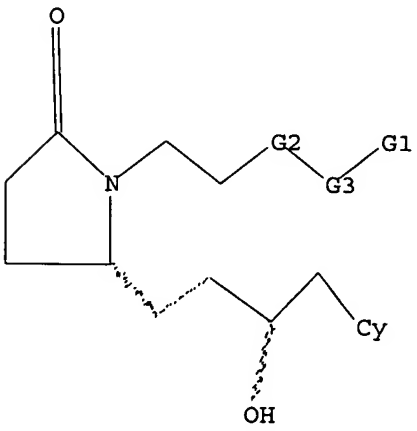
G2:O,CH2

G3:Ph,CH2,Hy,Ak

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:Atom 17:CLASS

L6 STRUCTURE UPLOADED

=> d l5
L5 HAS NO ANSWERS
L5 STR



G1 COOH,Hy

G2 O,CH2

G3 Ph,CH2,Hy,Ak

Structure attributes must be viewed using STN Express query preparation.

=> s l5
SAMPLE SEARCH INITIATED 10:57:20 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 113 TO ITERATE

100.0% PROCESSED 113 ITERATIONS 6 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1623 TO 2897
PROJECTED ANSWERS: 6 TO 266

L7 6 SEA SSS SAM L5

=> s l5 sss full
FULL SEARCH INITIATED 10:57:29 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 2090 TO ITERATE

100.0% PROCESSED 2090 ITERATIONS 141 ANSWERS
SEARCH TIME: 00.00.01

L8 141 SEA SSS FUL L5

=> FIL CAPLUS
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	161.76	331.84

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-0.73

FILE 'CAPLUS' ENTERED AT 10:57:33 ON 25 JAN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 25 Jan 2005 VOL 142 ISS 5
FILE LAST UPDATED: 24 Jan 2005 (20050124/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 18
L9 18 L8

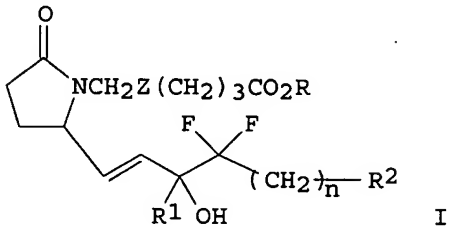
=> s l9 and py<=2000
20649267 PY<=2000
L10 3 L9 AND PY<=2000

=> d l10 ibib abs hitstr tot

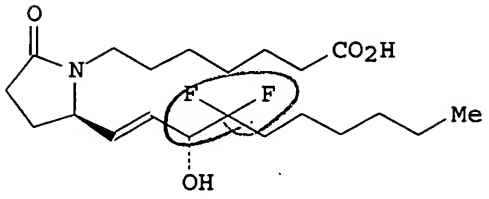
L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:438745 CAPLUS
DOCUMENT NUMBER: 97:38745
TITLE: 8-Aza-16,16-difluoroprostanoids
INVENTOR(S): Scribner, Richard Merrill
PATENT ASSIGNEE(S): du Pont de Nemours, E. I., and Co., USA
SOURCE: Eur. Pat. Appl., 64 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 46082	A2	19820217	EP 1981-303641	19810810 <--
EP 46082	A3	19820303		
EP 46082	B1	19850605		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4320136	A	19820316	US 1980-176784	19800811 <--
CA 1161447	A1	19840131	CA 1981-383299	19810806 <--
DK 8103522	A	19820212	DK 1981-3522	19810807 <--
JP 57054166	A2	19820331	JP 1981-124205	19810810 <--
AT 13667	E	19850615	AT 1981-303641	19810810 <--

PRIORITY APPLN. INFO.: US 1980-176784 A 19800811
EP 1981-303641 A 19810810
OTHER SOURCE(S): CASREACT 97:38745
GI



I

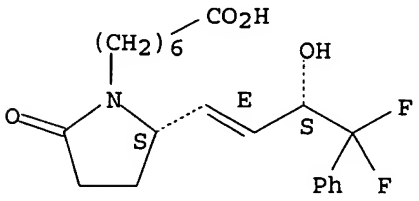


II

AB Racemic and optically active I [Z = CH2CH2, CH:CH, C.tplbond.C; R = H, C1-12 alkyl, cycloalkyl; R1 = H, Me, Et; R2 = Me, CF3, (un)substituted phenyl; n = 0-2 if R2 = aryl and 3-8 if R2 = Me or CF3] and their salts were prepared by appropriate modification of conventional methods. Typical of compds. prepared was II, whose Me ester gave better short-term gastric protection than PGE1 and at 5 mg/kg gave 80% protection against histamine-induced bronchoconstriction at 2 h orally.

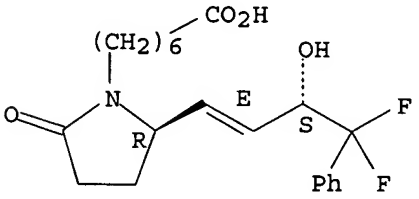
IT **82303-00-2P 82303-08-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 82303-00-2 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



RN 82303-08-0 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



L10 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1980:146340 CAPLUS
DOCUMENT NUMBER: 92:146340
TITLE: 1,5-Disubstituted-2-pyrrolidones
INVENTOR(S): Nelson, Albin J.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 19 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

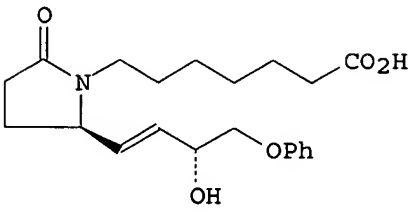
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4177346	A	19791204	US 1978-885908	19780313 <--
SE 7708642	A	19780207	SE 1977-8642	19770727 <--
SE 423813	B	19820607		
SE 423813	C	19820916		
CA 1077948	A1	19800520	CA 1977-283598	19770727 <--
IL 52615	A1	19810913	IL 1977-52615	19770728 <--
AU 7727515	A1	19790208	AU 1977-27515	19770801 <--
AU 508007	B2	19800306		
NL 7708637	A	19780208	NL 1977-8637	19770804 <--

ZA 7704704	A	19780628	ZA 1977-4704	19770804 <--
BE 857506	A1	19780206	BE 1977-8318	19770805 <--
DK 7703520	A	19780207	DK 1977-3520	19770805 <--
FI 7702376	A	19780207	FI 1977-2376	19770805 <--
FI 70009	B	19860131		
FI 70009	C	19860912		
NO 7702752	A	19780207	NO 1977-2752	19770805 <--
FR 2369260	A1	19780526	FR 1977-24290	19770805 <--
FR 2369260	B1	19820212		
ES 461388	A1	19781201	ES 1977-461388	19770805 <--
DD 136135	C	19790620	DD 1977-200468	19770805 <--
GB 1556569	A	19791128	GB 1977-33002	19770805 <--
GB 1556570	A	19791128	GB 1978-43588	19770805 <--
SU 703016	D	19791205	SU 1977-2511155	19770805 <--
DD 143768	C	19800910	DD 1977-213369	19770805 <--
CH 624934	A	19810831	CH 1977-9646	19770805 <--
HU 22714	O	19820628	HU 1977-PI587	19770805 <--
HU 180273	B	19830228		
CS 221269	P	19830429	CS 1977-5202	19770805 <--
JP 53021159	A2	19780227	JP 1977-94589	19770806 <--
JP 55031147	B4	19800815		
AT 7705794	A	19801115	AT 1977-5794	19770808 <--
AT 362887	B	19810625		
PL 112931	B1	19801129	PL 1977-215666	19770808 <--
RO 72530	P	19820201	RO 1977-91464	19770826 <--
ES 471349	A1	19790916	ES 1978-471349	19780701 <--
SU 818480	A3	19810330	SU 1978-2672200	19781011 <--
SU 850000	A3	19810723	SU 1978-2674602	19781017 <--
JP 55055161	A2	19800422	JP 1979-112743	19790903 <--
JP 58005196	B4	19830129		
CA 1084939	A2	19800902	CA 1980-343178	19800107 <--
DK 8004725	A	19801107	DK 1980-4725	19801107 <--
DK 146179	B	19830718		
DK 146179	C	19831212		

PRIORITY APPLN. INFO.:

US 1976-712362	A2	19760806
CA 1977-283598	A3	19770727
DK 1977-3520	A	19770805

GI



I

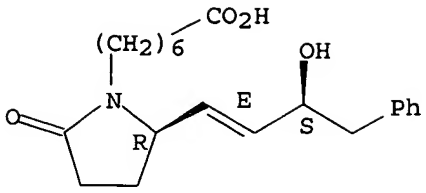
AB A series of known 8-azaprostaglandins (e.g., I) was prepared conventionally.

IT **66598-57-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and protection with dihydropyran)

RN 66598-57-0 CAPLUS

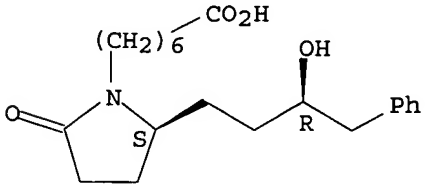
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **66598-64-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 66598-64-9 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-phenylbutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1978:405993 CAPLUS
DOCUMENT NUMBER: 89:5993
TITLE: 1,5-Disubstituted 2-pyrrolidones
INVENTOR(S): Nelson, Albin James
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Ger. Offen., 82 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

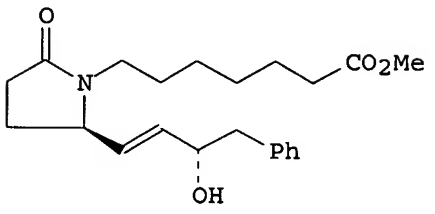
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2735904	A1	19780209	DE 1977-2735904	19770805 <--
SE 7708642	A	19780207	SE 1977-8642	19770727 <--
SE 423813	B	19820607		
SE 423813	C	19820916		
CA 1077948	A1	19800520	CA 1977-283598	19770727 <--
IL 52615	A1	19810913	IL 1977-52615	19770728 <--
AU 7727515	A1	19790208	AU 1977-27515	19770801 <--
AU 508007	B2	19800306		
NL 7708637	A	19780208	NL 1977-8637	19770804 <--
ZA 7704704	A	19780628	ZA 1977-4704	19770804 <--
BE 857506	A1	19780206	BE 1977-8318	19770805 <--
DK 7703520	A	19780207	DK 1977-3520	19770805 <--
FI 7702376	A	19780207	FI 1977-2376	19770805 <--
FI 70009	B	19860131		
FI 70009	C	19860912		
NO 7702752	A	19780207	NO 1977-2752	19770805 <--

FR 2369260	A1	19780526	FR 1977-24290	19770805 <--
FR 2369260	B1	19820212		
ES 461388	A1	19781201	ES 1977-461388	19770805 <--
DD 136135	C	19790620	DD 1977-200468	19770805 <--
GB 1556569	A	19791128	GB 1977-33002	19770805 <--
GB 1556570	A	19791128	GB 1978-43588	19770805 <--
SU 703016	D	19791205	SU 1977-2511155	19770805 <--
DD 143768	C	19800910	DD 1977-213369	19770805 <--
CH 624934	A	19810831	CH 1977-9646	19770805 <--
HU 22714	O	19820628	HU 1977-PI587	19770805 <--
HU 180273	B	19830228		
CS 221269	P	19830429	CS 1977-5202	19770805 <--
JP 53021159	A2	19780227	JP 1977-94589	19770806 <--
JP 55031147	B4	19800815		
AT 7705794	A	19801115	AT 1977-5794	19770808 <--
AT 362887	B	19810625		
PL 112931	B1	19801129	PL 1977-215666	19770808 <--
RO 72530	P	19820201	RO 1977-91464	19770826 <--
ES 471349	A1	19790916	ES 1978-471349	19780701 <--
SU 818480	A3	19810330	SU 1978-2672200	19781011 <--
SU 850000	A3	19810723	SU 1978-2674602	19781017 <--
JP 55055161	A2	19800422	JP 1979-112743	19790903 <--
JP 58005196	B4	19830129		
CA 1084939	A2	19800902	CA 1980-343178	19800107 <--
DK 8004725	A	19801107	DK 1980-4725	19801107 <--
DK 146179	B	19830718		
DK 146179	C	19831212		

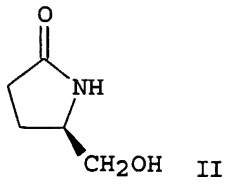
PRIORITY APPLN. INFO.:

US 1976-712362	A	19760806
CA 1977-283598	A3	19770727
DK 1977-3520	A	19770805

GI



I



II

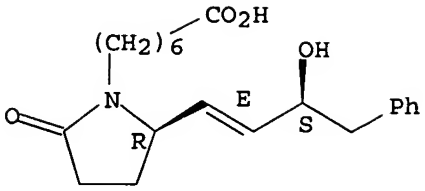
AB A series of 29 8-azaprostaglandins and intermediates for them, e.g. I, was prepared from (+)-II by, e.g., protecting with dihydropyran, alkylating with, e.g., Br(CH2)6CO2Et, deprotecting, oxidizing the CH2OH group to the aldehyde, condensing with the appropriate phosphorus ylide, and reducing with borohydride.

IT **66598-57-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and protection with dihydropyran)

RN 66598-57-0 CAPLUS

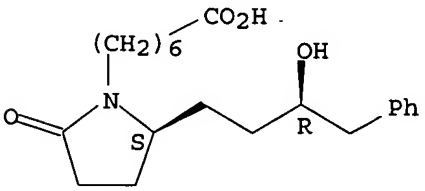
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



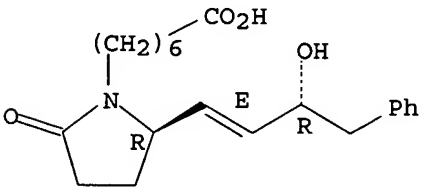
IT **66598-64-9P 66598-69-4P 66598-72-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 66598-64-9 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-phenylbutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



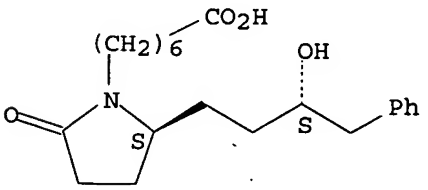
RN 66598-69-4 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3R)-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 66598-72-9 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3S)-3-hydroxy-4-phenylbutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d 19 ibib abs hitstr tot

L9 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:370901 CAPLUS
DOCUMENT NUMBER: 140:391154
TITLE: A preparation of pyrrolidinone derivatives useful as selective EP4 receptor agonists
INVENTOR(S): Billot, Xavier; Beunard, Jean-Luc; Han, Yongxin; Young, Robert N.; Colucci, John; Girard, Mario; Wilson, Marie-Claire
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037786	A2	20040506	WO 2003-CA1620	20031023
WO 2004037786	A3	20040930		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-421402P P 20021025
OTHER SOURCE(S): MARPAT 140:391154
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

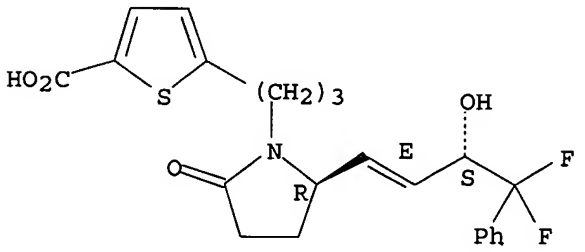
AB The invention relates to pyrrolidinone derivs. of formula I [wherein: Y1 = (CH2)2, CH:CH, 1,2-cyclopropanediyl; Y is C(O) or CH(OH); A is (CH2)1-4; Z = O, S, 1,2-cyclopropanediyl, HC:CH, C.tplbond.C, or a bond; Q is a disubstituted (hetero)aryl ring; W is a bond, unsubstituted C1-6 alkylene, or C1-6 alkylene substituted with 1-4 halogen atoms; R1 = OH, CN, CHO, etc.; R2 = C1-6alkyl, (CH2)0-8-(C6-10aryl), O-C1-10alkyl, etc.; R3 and R4 are independently selected from halogen, C1-6alkyl, or R3 and R4, together with the carbon atom to which they are attached, form a C3-7 cycloalkyl ring] useful as potent selective agonists of the EP4 subtype of prostaglandin E2 receptors. The invention compds. are useful in treatment of glaucoma and other conditions which are related to the elevated intraocular pressure in the eye. The invention relates to the use of the invention compds. for mediating the bone modeling and remodeling processes of the osteoblasts and osteoclasts. The invention compds. were tested as EP4 agonists on intraocular pressure in rabbits and monkeys; prostanoid receptor binding assays and bone resorption assays were performed (in a subclass of the invented compds., agonists have EC50 values from 0.01 μM to 10 μM). The synthesized stereoisomeric pyrrolidinones II were

prepared from pyrrole derivative III via oxidation, condensation with PhCF2C(O)CH2P(O)(OMe)2, keto-group reduction of the obtained unsatd. ketone IV, alc. protection, N-cleavage, addition of thiophene derivative V to the obtained compound VI, separation of the isomers, alc. deprotection, and hydrolysis.

IT **685896-00-8P 685896-02-0P 685896-04-2P**
685896-05-3P 685896-06-4P 685896-07-5P
685896-08-6P 685896-09-7P 685896-12-2P
685896-15-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidinone derivs. useful as selective EP4 receptor agonists)

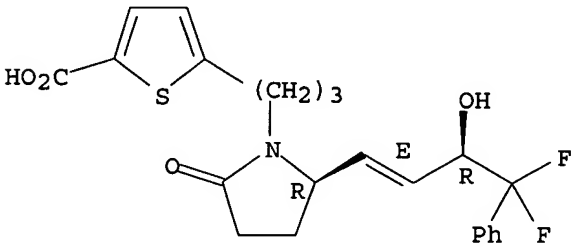
RN 685896-00-8 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2R)-2-[(1E,3S)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



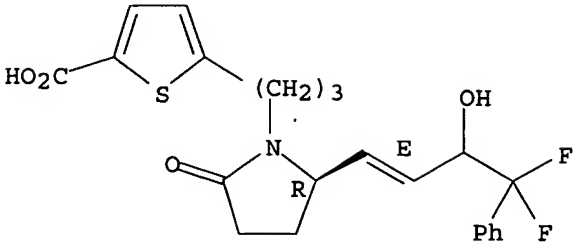
RN 685896-02-0 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2R)-2-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



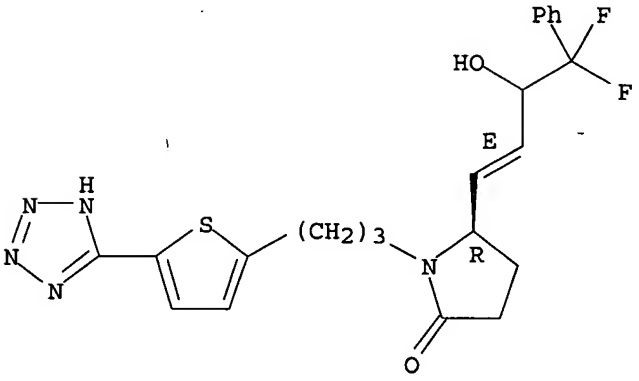
RN 685896-04-2 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2R)-2-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



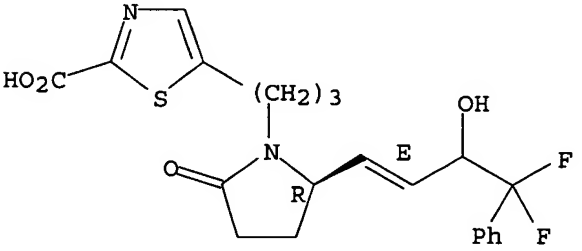
RN 685896-05-3 CAPLUS
CN 2-Pyrrolidinone, 5-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-1-[3-[5-(1H-tetrazol-5-yl)-2-thienyl]propyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



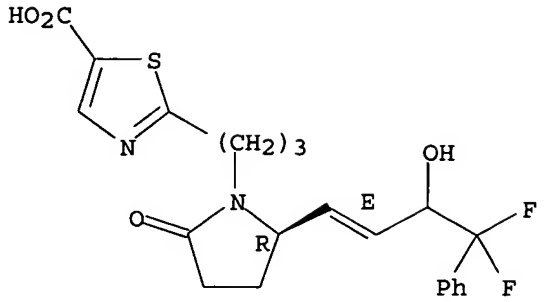
RN 685896-06-4 CAPLUS
CN 2-Thiazolecarboxylic acid, 5-[3-[(2R)-2-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



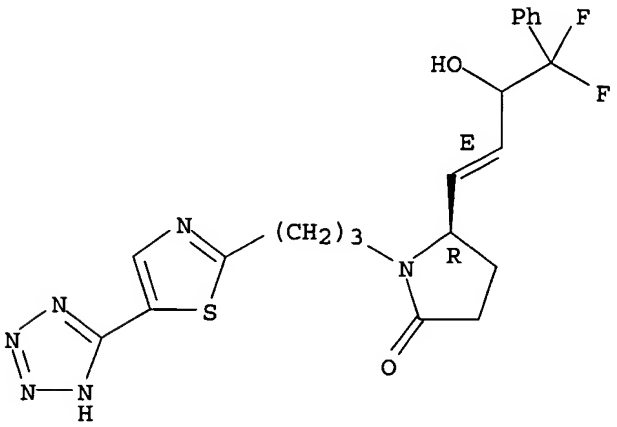
RN 685896-07-5 CAPLUS
CN 5-Thiazolecarboxylic acid, 2-[3-[(2R)-2-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



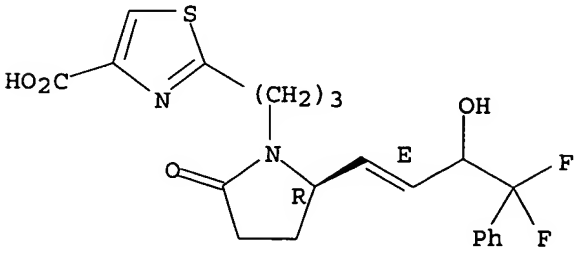
RN 685896-08-6 CAPLUS
CN 2-Pyrrolidinone, 5-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-1-[3-[5-(1H-tetrazol-5-yl)-2-thiazolyl]propyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



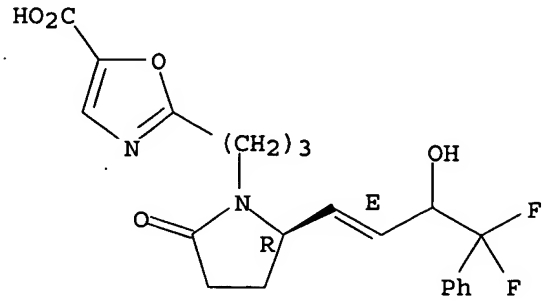
RN 685896-09-7 CAPLUS
CN 4-Thiazolecarboxylic acid, 2-[3-[(2R)-2-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



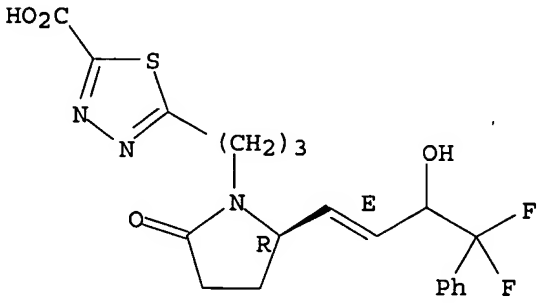
RN 685896-12-2 CAPLUS
CN 5-Oxazolecarboxylic acid, 2-[3-[(2R)-2-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

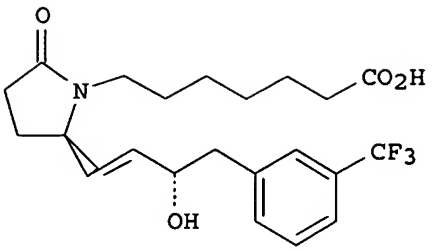


RN 685896-15-5 CAPLUS
CN 1,3,4-Thiadiazole-2-carboxylic acid, 5-[3-[(2R)-2-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L9 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:214102 CAPLUS
DOCUMENT NUMBER: 141:6940
TITLE: Lactams as EP4 prostanoid receptor subtype selective agonists. Part 1: 2-Pyrrolidinones-stereochemical and lower side-chain optimization
AUTHOR(S): Elworthy, Todd R.; Kertesz, Denis J.; Kim, Woongki; Roepel, Michael G.; Quattrocchio-Setti, Lina; Smith, David B.; Tracy, Jahari Laurant; Chow, Audrey; Li, Fujun; Brill, Emma R.; Lach, Leang K.; McGee, Daren; Yang, Diana S.; Chiou, San-San
CORPORATE SOURCE: Department of Medicinal Chemistry, Roche Palo Alto, Palo Alto, CA, 94304-1397, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(7), 1655-1659
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:6940
GI



I

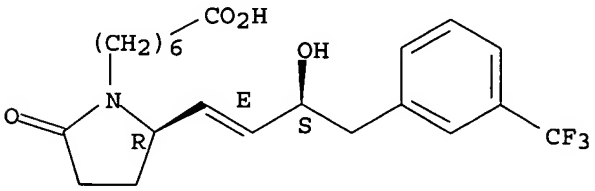
AB A series of 7-[(5R)-substituted 2-oxo-1-pyrrolidinyl]heptanoic acids were prepared, their isomeric purity determined, and pharmacol. evaluated. Lactams with affinity for the EP4 receptor displayed agonist behavior. The lower side-chain of the lactam template could be substituted to afford ligands (e.g., I) of high potency and greater than 1000-fold affinity for EP4 vs. the other EP prostanoid receptors.

IT **494221-79-3P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 7-[(5R)-substituted 2-oxo-1-pyrrolidinyl]heptanoic acids as EP4 receptor agonists)

RN 494221-79-3 CAPLUS

CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-[3-(trifluoromethyl)phenyl]-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

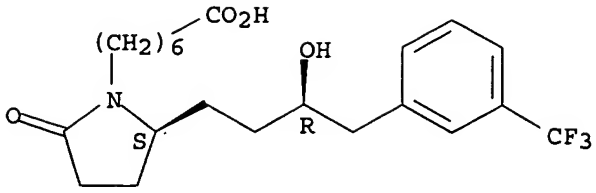


IT **346672-61-5P 356528-12-6P 695231-40-4P**
695231-41-5P 695231-42-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of 7-[(5R)-substituted 2-oxo-1-pyrrolidinyl]heptanoic acids as EP4 receptor agonists)

RN 346672-61-5 CAPLUS

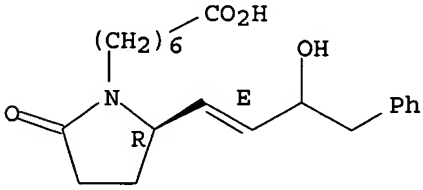
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



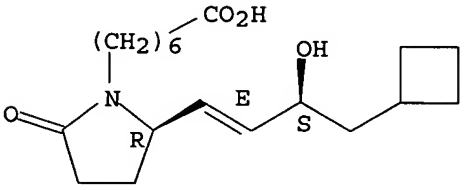
RN 356528-12-6 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E)-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



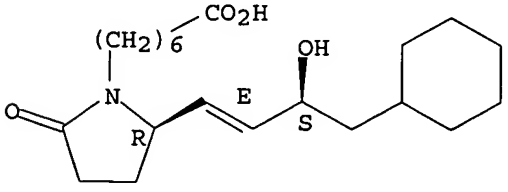
RN 695231-40-4 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-4-cyclobutyl-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 695231-41-5 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-4-cyclohexyl-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

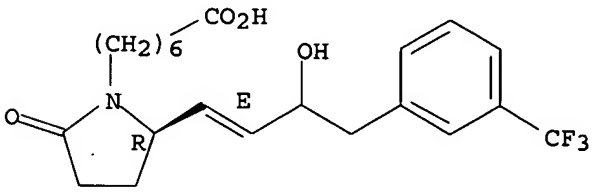
Absolute stereochemistry.
Double bond geometry as shown.



RN 695231-42-6 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E)-3-hydroxy-4-[3-

(trifluoromethyl)phenyl]-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:991395 CAPLUS
DOCUMENT NUMBER: 140:23287
TITLE: 2-Pyrrolidinone derivatives for use as EP4 receptor agonists in the treatment of eye diseases such as glaucoma
INVENTOR(S): Billot, Xavier; Young, Robert N.; Han, Yongxin
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003103772	A1	20031218	WO 2003-CA838	20030602

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-386499P P 20020606
US 2003-460134P P 20030403

OTHER SOURCE(S): MARPAT 140:23287

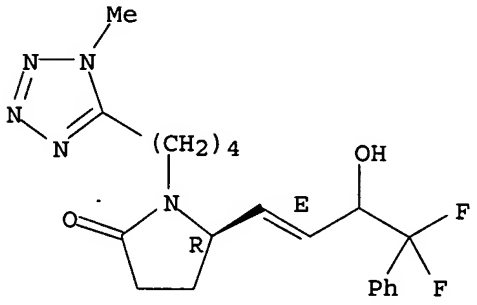
AB This invention relates to 1,5-disubstituted 2-pyrrolidinone derivs. as potent selective agonists of the EP4 subtype of prostaglandin E2 receptors, topical formulations containing the same, and their use in the treatment of glaucoma and other conditions which are related to elevated intraocular pressure in the eye of the patient.

IT **634193-15-0P 634193-17-2P 634193-19-4P**
634193-20-7P 634193-28-5P 634193-29-6P
634193-31-0P 634193-34-3P 634193-36-5P
634193-39-8P 634193-43-4P 634193-46-7P
634193-47-8P 634193-54-7P 634193-66-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(ophthalmic compns. containing pyrrolidinone derivs. as EP4 receptor agonists for treatment of eye diseases)

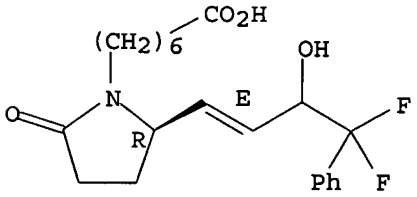
RN 634193-15-0 CAPLUS
CN 2-Pyrrolidinone, 5-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-1-[4-(1-methyl-1H-tetrazol-5-yl)butyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



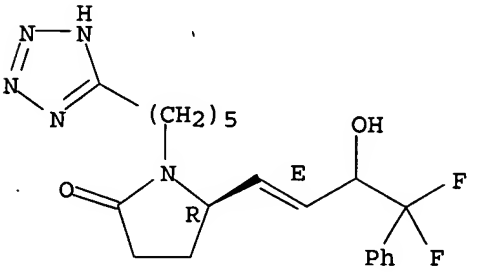
RN 634193-17-2 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 634193-19-4 CAPLUS
CN 2-Pyrrolidinone, 5-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-1-[5-(1H-tetrazol-5-yl)pentyl]-, (5R)- (9CI) (CA INDEX NAME)

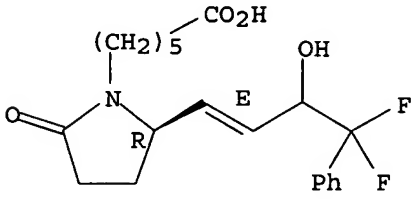
Absolute stereochemistry.
Double bond geometry as shown.



RN 634193-20-7 CAPLUS
CN 1-Pyrrolidinehexanoic acid, 2-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-

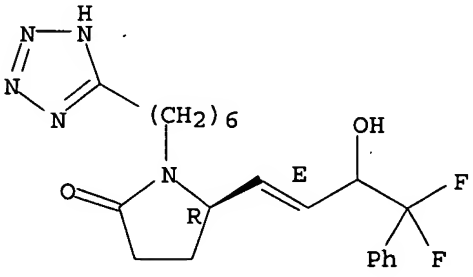
butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



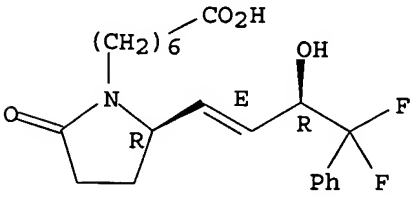
RN 634193-28-5 CAPLUS
CN 2-Pyrrolidinone, 5-[(1E)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



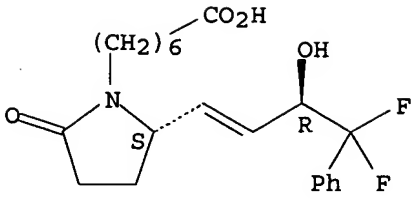
RN 634193-29-6 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



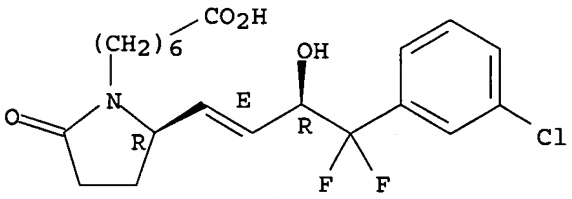
RN 634193-31-0 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



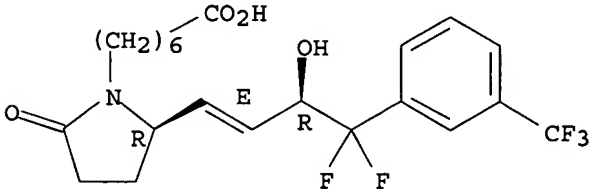
RN 634193-34-3 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3R)-4-(3-chlorophenyl)-4,4-difluoro-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



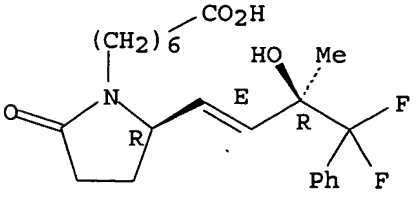
RN 634193-36-5 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3R)-4,4-difluoro-3-hydroxy-4-[3-(trifluoromethyl)phenyl]-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 634193-39-8 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3R)-4,4-difluoro-3-hydroxy-3-methyl-4-phenyl-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

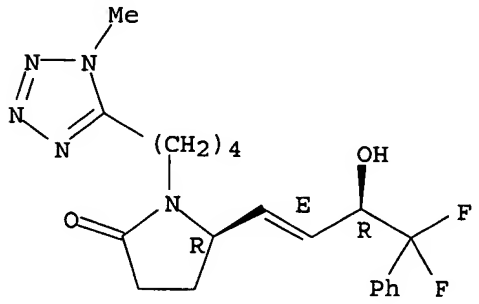
Absolute stereochemistry.
Double bond geometry as shown.



RN 634193-43-4 CAPLUS
CN 2-Pyrrolidinone, 5-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-1-

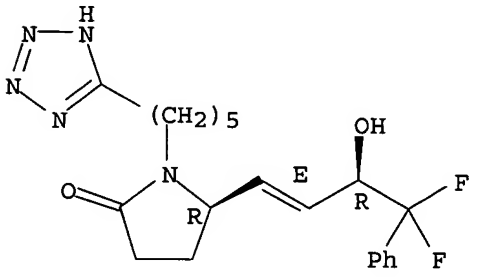
[4-(1-methyl-1H-tetrazol-5-yl)butyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



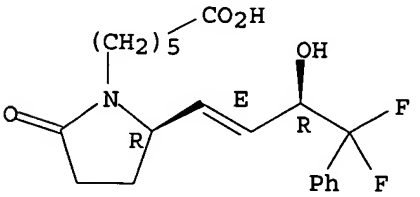
RN 634193-46-7 CAPLUS
CN 2-Pyrrolidinone, 5-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-1-[5-(1H-tetrazol-5-yl)pentyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



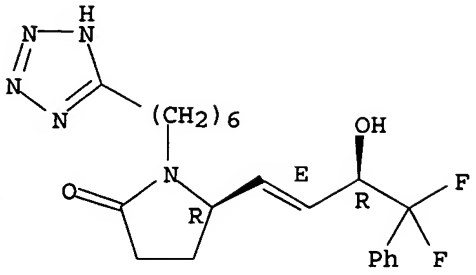
RN 634193-47-8 CAPLUS
CN 1-Pyrrolidinehexanoic acid, 2-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



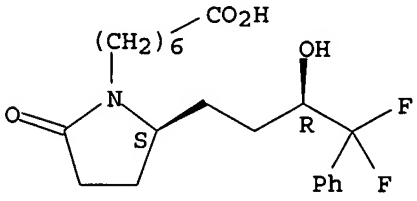
RN 634193-54-7 CAPLUS
CN 2-Pyrrolidinone, 5-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 634193-66-1 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-4,4-difluoro-3-hydroxy-4-phenylbutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

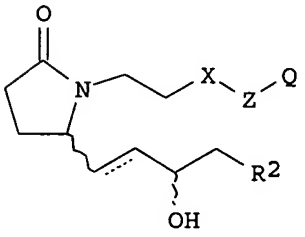
L9 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:757519 CAPLUS
DOCUMENT NUMBER: 139:276812
TITLE: Preparation of hydroxyorgano pyrrolidinones as EP4 receptor selective agonists for the treatment of hypertension and other disorders
INVENTOR(S): Cameron, Kimberly O'Keefe; Lefker, Bruce Allen; Knight, Delvin Roscoe, Jr.
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003077910	A1	20030925	WO 2003-IB844	20030306
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1487437	A1	20041222	EP 2003-704902	20030306

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

US 2003207925 A1 20031106 US 2003-386307 20030311
PRIORITY APPLN. INFO.: US 2002-365711P P 20020318
WO 2003-IB844 W 20030306
OTHER SOURCE(S): MARPAT 139:276812

GI



I

AB This invention is directed to hydroxyorgano pyrrolidinones (I; e.g. 4-[3-[2-(3-hydroxy-4-phenylbutyl)-5-oxopyrrolidin-1-yl]propyl]benzoic acid; R2, X, Z and Q are defined below and in more detail in the claims) that are EP4 receptor selective prostaglandin agonists. This invention is also directed to pharmaceutical compns. containing those compds. This invention is also directed to methods of treating hypertension, liver failure, loss of patency of the ductus arteriosus, glaucoma or ocular hypertension. IC50 values for binding of 5-[3-[2S-[3R-hydroxy-4-(3-trifluoromethylphenyl)butyl]-5-oxopyrrolidin-1-yl]propyl]thiophene-2-carboxylic acid (II) to various receptors are human EP1 receptor, >1000 nm; rat EP2 receptor, 463 nm; human EP3 receptor, > 1000 nm; and rat EP4 receptor, 11 nm. II exhibited an EC50 value of 0.6 nm in an assay involving cAMP elevation in 293S cell lines stably overexpressing recombinant rat EP4 receptors. Results are also presented for the hypotensive effect of the Na salt of II in in vivo rabbit and primate models. In I, a prodrug thereof, a pharmaceutically acceptable salt of said compound or said prodrug or a stereoisomer or diastereomeric mixture of said compound, prodrug or salt: the dotted line is a bond or no bond; X is -CH2- or O; Z is -(CH2)3-, thienyl, thiazolyl or Ph, provided that when X is O, then Z is phenyl; Q is carboxy, (C1-C4)alkoxycarbonyl or tetrazolyl; R2 is -Ar or -Ar1-V-Ar2; V is a bond, -O-, -OCH2- or -CH2O-. Ar is a partially saturated, fully saturated or fully unsatd. 5-8 membered ring optionally having 1-4 heteroatoms selected independently from O, S and N, or a bicyclic ring consisting of two fused independently partially saturated, fully saturated or fully unsatd. 5-6 membered rings, taken independently, optionally having 1-4 heteroatoms selected independently from N, S and O, said partially or fully saturated ring or bicyclic ring optionally having 1-2 oxo groups substituted on C or 1-2 oxo groups substituted on S. Ar1 and Ar2 are each independently a partially saturated, fully saturated or fully unsatd. 5-8 membered ring optionally having 1-4 heteroatoms selected independently from O, S and N, said partially or fully saturated ring optionally having 1-2 oxo groups substituted on C or 1-2 oxo groups substituted on S. Ar is optionally substituted on C or N, on one ring if the moiety is monocyclic, or on one or both rings if the moiety is bicyclic, with up to three substituents per ring each independently selected from hydroxy, halo, carboxy, (C1-C7) alkoxy, (C1-C4)alkoxy(C1-C4)alkyl, (C1-C7)alkyl,

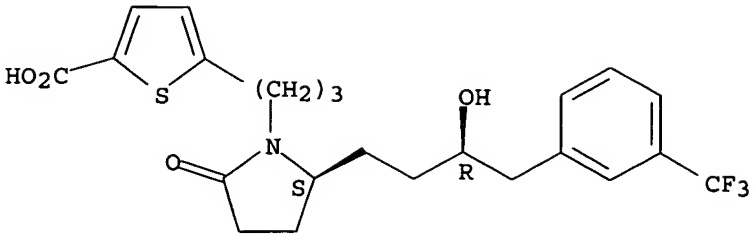
(C2-C7)alkenyl, (C3-C7)cycloalkyl, (C3-C7)cycloalkyl(C1-C4)alkyl, (C3-C7)cycloalkyl(C1-C4)alkanoyl, formyl, (C1-C8) alkanoyl, (C1-C6)alkanoyl(C1-C6)alkyl, (C1-C4)alkanoylamino, (C1-C4)alkoxycarbonylamino, hydroxysulfonyl, aminocarbonylamino or mono-N-, di-N,N-, di-N,N'- or tri-N,N,N'-(C1-C4)alkyl substituted aminocarbonylamino, sulfonamido, (C1-C4)alkylsulfonamido, amino, mono-N- or di-N,N-(C1-C4)alkylamino, carbamoyl, mono-N- or di-N,N-(C1-C4)alkylcarbamoyl, cyano, thiol, (C1-C6)alkylthio, (C1-C6)alkylsulfinyl, (C1-C4)alkylsulfonyl and mono-N- or di-N,N-(C1-C4)alkylaminosulfinyl, wherein said alkyl and alkoxy substituents in the definition of Ar are optionally substituted on C with up to three fluoro. Ar1 and Ar2 are independently optionally substituted on C or N with up to three substituents each independently selected from hydroxy, halo, carboxy, (C1-C7)alkoxy, (C1-C4)alkoxy(C1-C4)alkyl, (C1-C7)alkyl, (C2-C7)alkenyl, (C3-C7)cycloalkyl, (C3-C7)cycloalkyl(C1-C4)alkyl, (C3-C7)cycloalkyl(C1-C4)alkanoyl, formyl, (C1-C8)alkanoyl, (C1-C6)alkanoyl(C1-C6)alkyl, (C1-C4)alkanoylamino, (C1-C4)alkoxycarbonylamino, hydroxysulfonyl, aminocarbonylamino or mono-N-, di-N,N-, di-N,N'- or tri-N,N,N'-(C1-C4)alkyl substituted aminocarbonylamino, sulfonamido, (C1-C4)alkylsulfonamido, amino, mono-N- or di-N,N-(C1-C4)alkylamino, carbamoyl, mono-N- or di-N,N-(C1-C4)alkylcarbamoyl, cyano, thiol, (C1-C6)alkylthio, (C1-C6)alkylsulfinyl, (C1-C4)alkylsulfonyl and mono-N- or di-N,N-(C1-C4)alkylaminosulfinyl, wherein said alkyl and alkoxy substituents in the definition of Ar1 and Ar2 are optionally substituted on C with up to three fluoro. (a) when X is (CH2)- and Z is -(CH2)3-, then R2 is not thienyl, Ph or Ph monosubstituted with chloro, fluoro, Ph, methoxy, trifluoromethyl or (C1-C4) alkyl; and (b) when X is (CH2)-, Z is -(CH2)3-, and Q is carboxy or (C1-C4) alkoxycarbonyl, then R2 is not (i) (C5-C7)cycloalkyl or (ii)phenyl, thienyl or furyl each of which may be optionally monosubstituted or disubstituted by one or two substituents selected, independently in the latter case, from halogen atoms, alkyl groups having 1-3 C atoms which may be substituted by one or more halogen atoms, and alkoxy groups having 1-4 C atoms. Although the methods of preparation are not claimed, 41 example prepns. are included.

IT **605686-01-9P**, 5-[3-[2S-[3R-Hydroxy-4-(3-trifluoromethylphenyl)butyl]-5-oxopyrrolidin-1-yl]propyl]thiophene-2-carboxylic acid sodium salt
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of hydroxyorgano pyrrolidinones as EP4 receptor selective agonists for treatment of hypertension and other disorders)

RN 605686-01-9 CAPLUS

CN 2-Thiophenecarboxylic acid, 5-[3-[(2S)-2-[(3R)-3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl]-5-oxo-1-pyrrolidinyl]propyl]-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



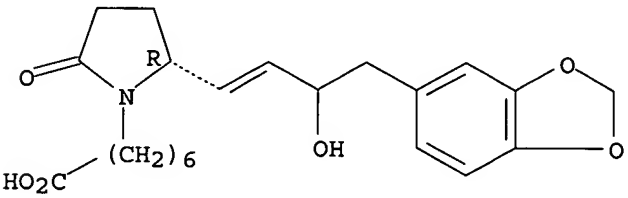
● Na

IT **431989-27-4P**, 7-[2R-(4-Benzo[1,3]dioxol-5-yl-3-hydroxybut-1-enyl)-5-oxopyrrolidin-1-yl]heptanoic acid **431990-16-8P** **431990-21-5P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(intermediate; preparation of hydroxyorgano pyrrolidinones as EP4 receptor selective agonists for treatment of hypertension and other disorders)

RN 431989-27-4 CAPLUS

CN 1-Pyrrolidineheptanoic acid, 2-[4-(1,3-benzodioxol-5-yl)-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

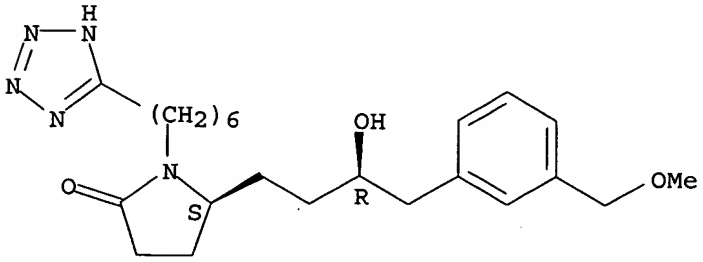
Absolute stereochemistry.
Double bond geometry unknown.



RN 431990-16-8 CAPLUS

CN 2-Pyrrolidinone, 5-[(3R)-3-hydroxy-4-[3-(methoxymethyl)phenyl]butyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

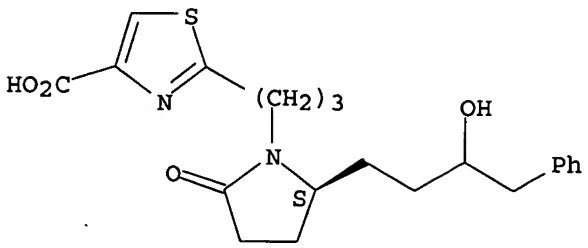
Absolute stereochemistry.



RN 431990-21-5 CAPLUS

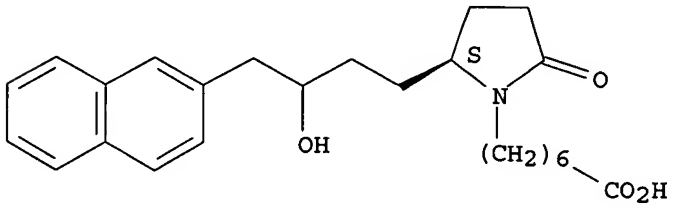
CN 4-Thiazolecarboxylic acid, 2-[3-[(2S)-2-(3-hydroxy-4-phenylbutyl)-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



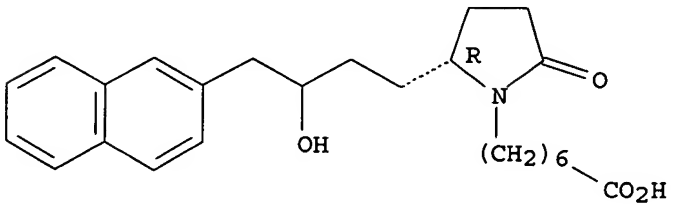
IT **431989-25-2P**, 7-[2S-(3-Hydroxy-4-naphthalen-2-ylbutyl)-5-oxopyrrolidin-1-yl]heptanoic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of hydroxyorgano pyrrolidinones as EP4 receptor selective agonists for treatment of hypertension and other disorders)
RN 431989-25-2 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[3-hydroxy-4-(2-naphthalenyl)butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **431989-21-8P**, 7-[2R-(3-Hydroxy-4-naphthalen-2-ylbutyl)-5-oxopyrrolidin-1-yl]heptanoic acid **431990-08-8P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of hydroxyorgano pyrrolidinones as EP4 receptor selective agonists for treatment of hypertension and other disorders)
RN 431989-21-8 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[3-hydroxy-4-(2-naphthalenyl)butyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

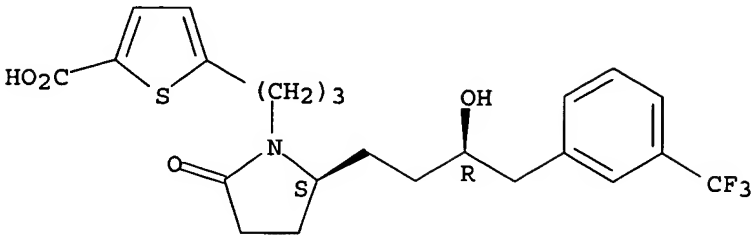
Absolute stereochemistry.



RN 431990-08-8 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2S)-2-[(3R)-3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA

INDEX NAME)

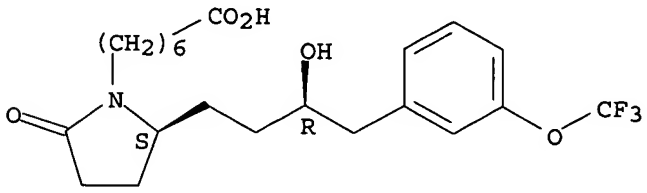
Absolute stereochemistry.



IT **346673-09-4P**, 7-[2S-[3R-Hydroxy-4-(3-trifluoromethoxyphenyl)butyl]-5-oxopyrrolidin-1-yl]heptanoic acid **431989-16-1P**, 7-[2S-[3R-Hydroxy-4-(3-methoxymethylphenyl)butyl]-5-oxopyrrolidin-1-yl]heptanoic acid **431989-26-3P 431989-29-6P 431989-30-9P**, 7-[2S-(4-Benzo[1,3]dioxol-5-yl-3-hydroxybutyl)-5-oxopyrrolidin-1-yl]heptanoic acid **431989-40-1P**, 7-[2S-[4-(3-Cyanophenyl)-3R-hydroxybutyl]-5-oxopyrrolidin-1-yl]heptanoic acid **431990-12-4P 431990-20-4P 431990-27-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of hydroxyorgano pyrrolidinones as EP4 receptor selective agonists for treatment of hypertension and other disorders)

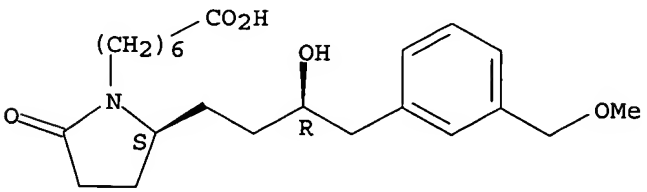
RN 346673-09-4 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-[3-(trifluoromethoxy)phenyl]butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



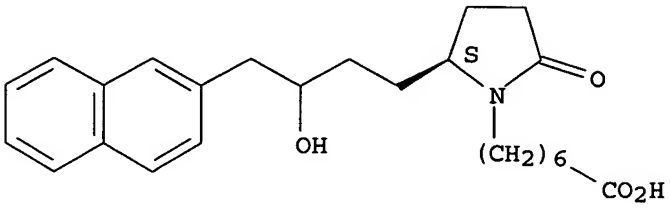
RN 431989-16-1 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-[3-(methoxymethyl)phenyl]butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 431989-26-3 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[3-hydroxy-4-(2-naphthalenyl)butyl]-5-oxo-, monosodium salt, (2S)- (9CI) (CA INDEX NAME)

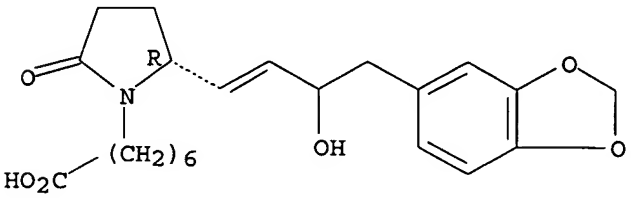
Absolute stereochemistry.



● Na

RN 431989-29-6 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[4-(1,3-benzodioxol-5-yl)-3-hydroxy-1-butenyl]-5-oxo-, monosodium salt, (2R)- (9CI) (CA INDEX NAME)

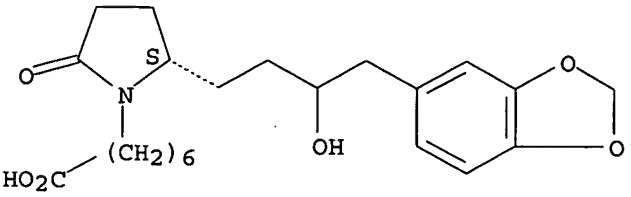
Absolute stereochemistry.
Double bond geometry unknown.



● Na

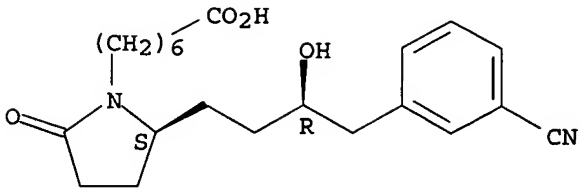
RN 431989-30-9 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[4-(1,3-benzodioxol-5-yl)-3-hydroxybutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



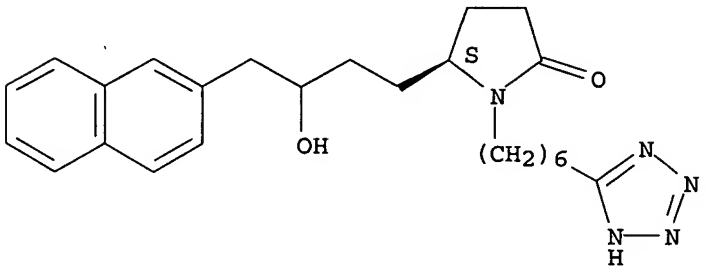
RN 431989-40-1 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-4-(3-cyanophenyl)-3-hydroxybutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



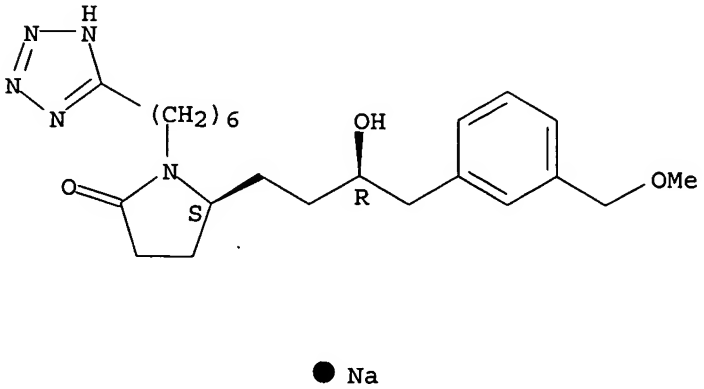
RN 431990-12-4 CAPLUS
CN 2-Pyrrolidinone, 5-[3-hydroxy-4-(2-naphthalenyl)butyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



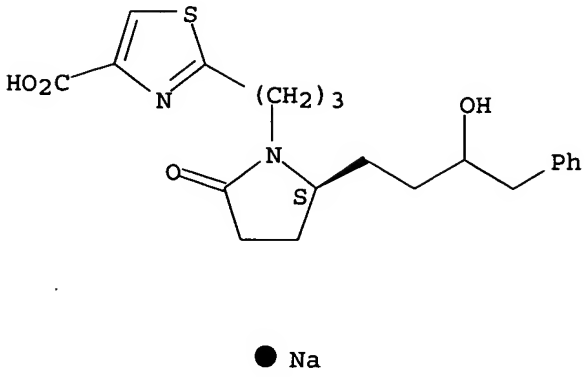
RN 431990-20-4 CAPLUS
CN 2-Pyrrolidinone, 5-[(3R)-3-hydroxy-4-[3-(methoxymethyl)phenyl]butyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, monosodium salt, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 431990-27-1 CAPLUS
CN 4-Thiazolecarboxylic acid, 2-[3-[(2S)-2-(3-hydroxy-4-phenylbutyl)-5-oxo-1-pyrrolidinyl]propyl]-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



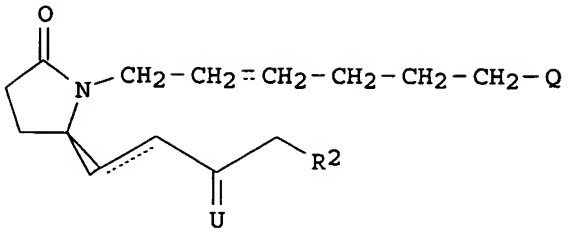
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:737375 CAPLUS
DOCUMENT NUMBER: 139:255396
TITLE: Use of selective EP4 receptor agonists for the treatment of liver failure, loss of patency of the ductus arteriosus, glaucoma or ocular hypertension
INVENTOR(S): Cameron, Kimberly O.; Lefker, Bruce A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 12 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003176479	A1	20030918	US 2003-386324	20030311
WO 2003077908	A1	20030925	WO 2003-IB955	20030306
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1490055	A1	20041229	EP 2003-744470	20030306
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: US 2002-365654P P 20020318
WO 2003-IB955 W 20030306

OTHER SOURCE(S): MARPAT 139:255396
GI



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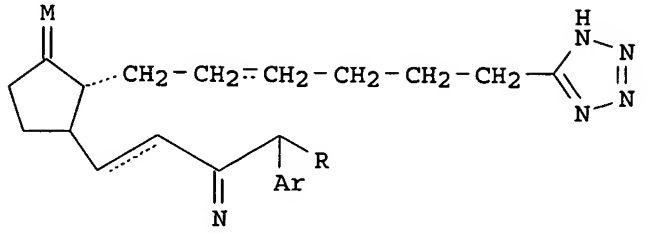


II

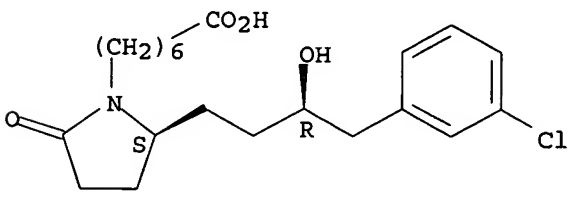
AB The invention discloses methods for treating liver failure, loss of patency of the ductus arteriosus, glaucoma or ocular hypertension, comprising administering to the patient in need thereof a therapeutically effective amount of a selective EP4 receptor agonist I (Q= COOR3, CONHR4, tetrazol-5-yl; A = single or cis double bond; B = single or trans double bond; =U = =O, etc.; R2 = α-thienyl, Ph, phenoxy, etc.; R3 = H, C1-5 alkyl, Ph, p-biphenyl; R4 = COR5 or SO2R5; R5 = Ph, C1-5 alkyl) or II (Ar = α- or β-thienyl, 5-phenyl-α- or β-thienyl, α- or β-naphthyl, tropyl, etc.; R = H, Me; W = single bond or cis double bond; Z = single bond or trans double bond; =M, =N = =O, etc.).

IT **346672-57-9 346672-61-5 346672-67-1 346672-71-7 346672-87-5 346672-93-3 356528-09-1 356528-10-4 356528-11-5 356528-12-6 600640-19-5 600640-21-9 600640-23-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(EP4 receptor agonists for treatment of liver failure, loss of patency of ductus arteriosus, glaucoma or ocular hypertension)

RN 346672-57-9 CAPLUS

CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-4-(3-chlorophenyl)-3-hydroxybutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

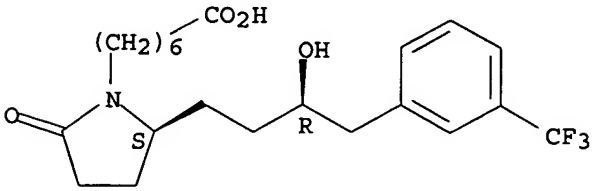


RN 346672-61-5 CAPLUS

CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-[3-

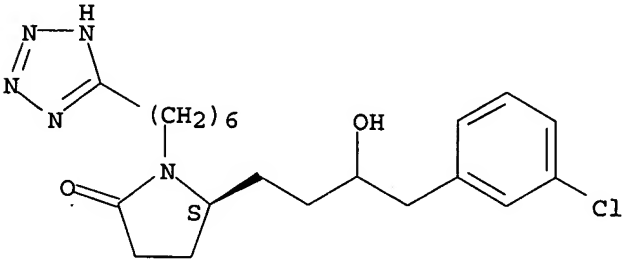
(trifluoromethyl)phenyl]butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



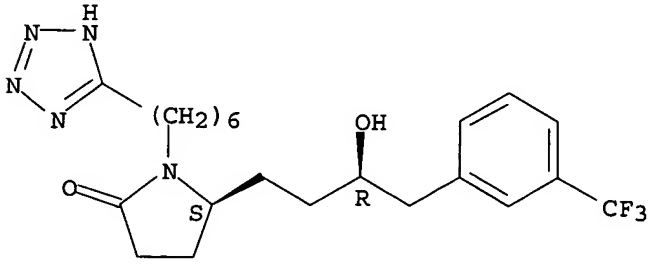
RN 346672-67-1 CAPLUS
CN 2-Pyrrolidinone, 5-[4-(3-chlorophenyl)-3-hydroxybutyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



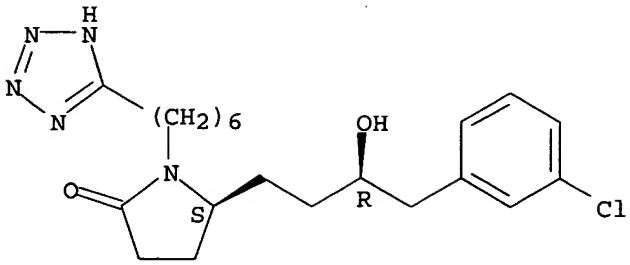
RN 346672-71-7 CAPLUS
CN 2-Pyrrolidinone, 5-[(3R)-3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



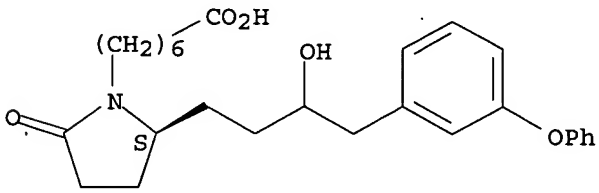
RN 346672-87-5 CAPLUS
CN 2-Pyrrolidinone, 5-[(3R)-4-(3-chlorophenyl)-3-hydroxybutyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



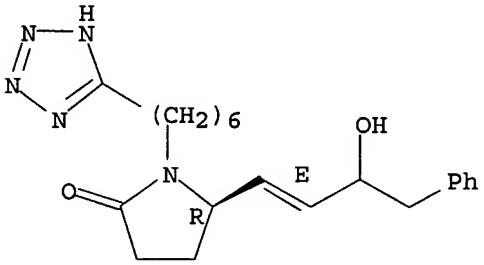
RN 346672-93-3 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[3-hydroxy-4-(3-phenoxyphenyl)butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



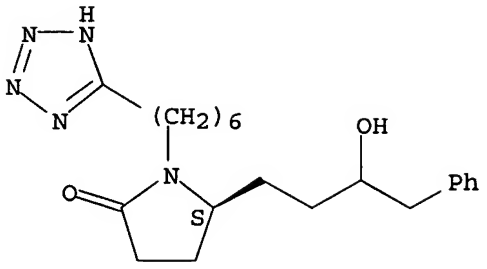
RN 356528-09-1 CAPLUS
CN 2-Pyrrolidinone, 5-[(1E)-3-hydroxy-4-phenyl-1-butenyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



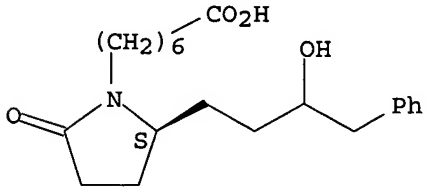
RN 356528-10-4 CAPLUS
CN 2-Pyrrolidinone, 5-(3-hydroxy-4-phenylbutyl)-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



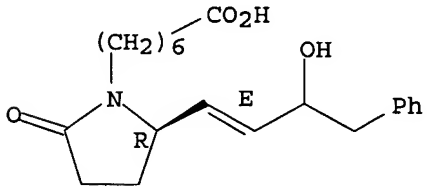
RN 356528-11-5 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-(3-hydroxy-4-phenylbutyl)-5-oxo-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



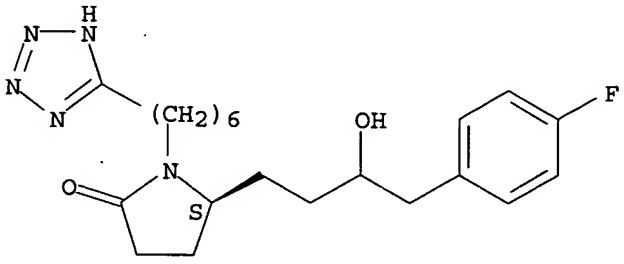
RN 356528-12-6 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E)-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



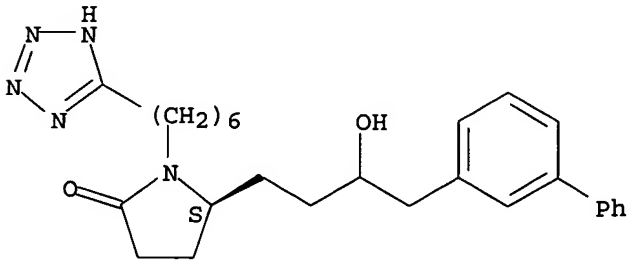
RN 600640-19-5 CAPLUS
CN 2-Pyrrolidinone, 5-[4-(4-fluorophenyl)-3-hydroxybutyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



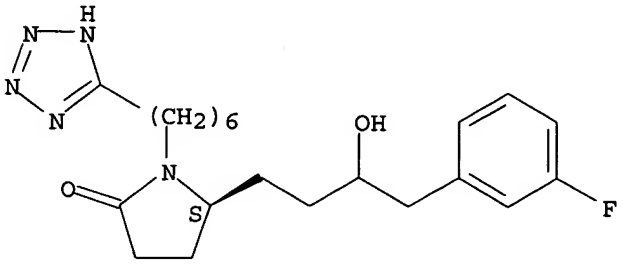
RN 600640-21-9 CAPLUS
CN 2-Pyrrolidinone, 5-(4-[1,1'-biphenyl]-3-yl-3-hydroxybutyl)-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 600640-23-1 CAPLUS
CN 2-Pyrrolidinone, 5-[4-(3-fluorophenyl)-3-hydroxybutyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:454063 CAPLUS
DOCUMENT NUMBER: 139:30848
TITLE: Method for treating ocular hypertension by using potent and selective agonists of the EP4 subtype of prostaglandin E2 receptors
INVENTOR(S): Ogidigben, Miller J.; Young, Robert N.; Metters, Kathleen M.; Slipetz, Deborah M.; Billot, Xavier
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Merck Frosst Canada & Co.
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003047513	A2	20030612	WO 2002-US38040	20021127
WO 2003047513	A3	20040715		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,

PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1461026	A2	20040929	EP 2002-784630		20021127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
US 2004254230	A1	20041216	US 2004-494775		20040504
PRIORITY APPLN. INFO.:			US 2001-338117P	P	20011203
			US 2002-400504P	P	20020802
			WO 2002-US38040	W	20021127

OTHER SOURCE(S): MARPAT 139:30848

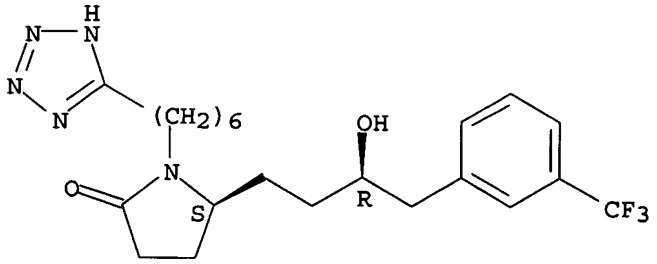
AB This invention relates to potent selective agonists of the EP4 subtype of prostaglandin E2 receptors, their use or a formulation thereof in the treatment of glaucoma and other conditions that are related to elevated intraocular pressure in the eye of a patient. This invention also relates to the use of such compds. to provide a neuroprotective effect to the eye of mammalian species, particularly humans.

IT **346672-71-7P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(treatment of ocular hypertension by using potent and selective agonists of the EP4 subtype of prostaglandin E2 receptors)

RN 346672-71-7 CAPLUS

CN 2-Pyrrolidinone, 5-[(3R)-3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

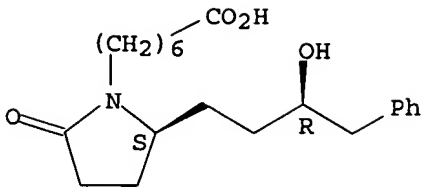


IT **66598-64-9P 346672-57-9P 346672-61-5P**
346672-67-1P 346672-80-8P 346672-87-5P
346673-06-1P 346673-07-2P 346673-08-3P
346673-10-7P 431989-51-4P 540731-22-4P
540731-32-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(treatment of ocular hypertension by using potent and selective agonists of the EP4 subtype of prostaglandin E2 receptors)

RN 66598-64-9 CAPLUS

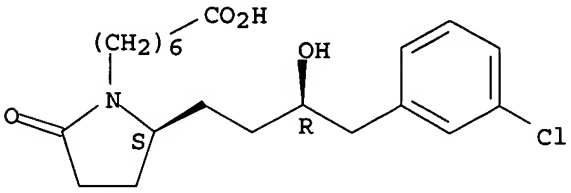
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-phenylbutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



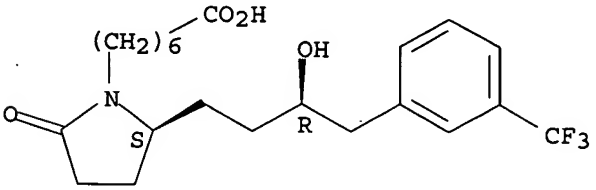
RN 346672-57-9 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-4-(3-chlorophenyl)-3-hydroxybutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



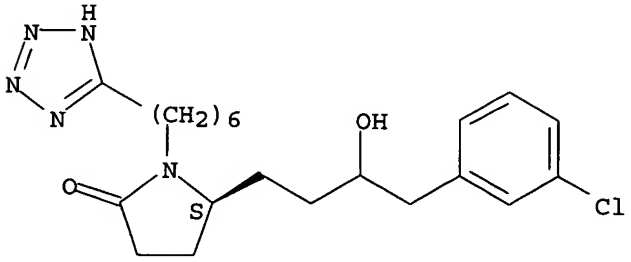
RN 346672-61-5 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

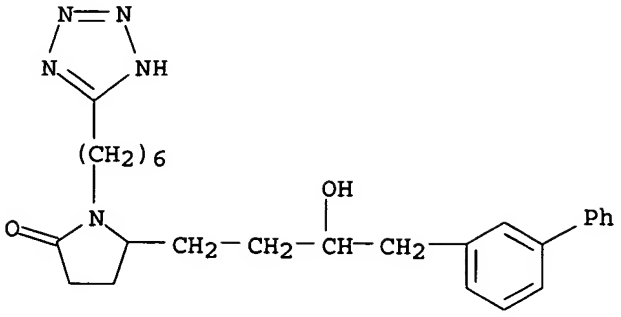


RN 346672-67-1 CAPLUS
CN 2-Pyrrolidinone, 5-[4-(3-chlorophenyl)-3-hydroxybutyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

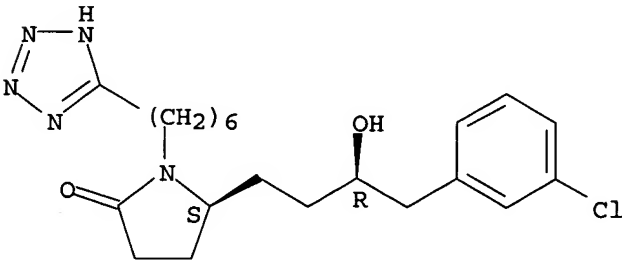


RN 346672-80-8 CAPLUS
CN 2-Pyrrolidinone, 5-(4-[1,1'-biphenyl]-3-yl-3-hydroxybutyl)-1-[6-(1H-tetrazol-5-yl)hexyl]- (9CI) (CA INDEX NAME)



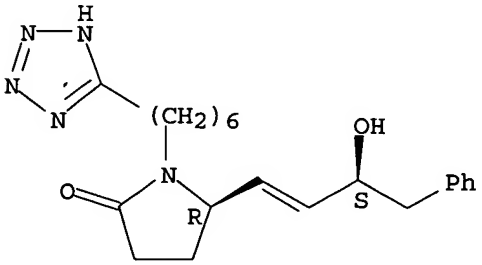
RN 346672-87-5 CAPLUS
CN 2-Pyrrolidinone, 5-[(3R)-4-(3-chlorophenyl)-3-hydroxybutyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



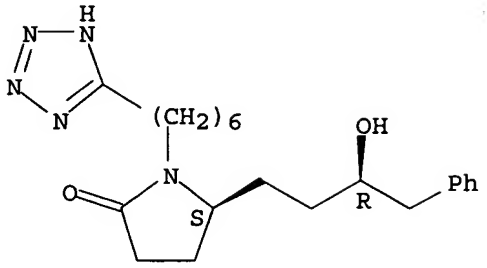
RN 346673-06-1 CAPLUS
CN 2-Pyrrolidinone, 5-[(3S)-3-hydroxy-4-phenyl-1-butenyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



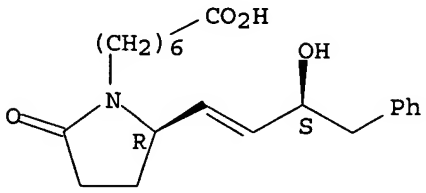
RN 346673-07-2 CAPLUS
CN 2-Pyrrolidinone, 5-[(3R)-3-hydroxy-4-phenylbutyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



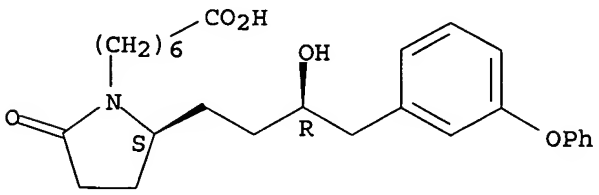
RN 346673-08-3 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3S)-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



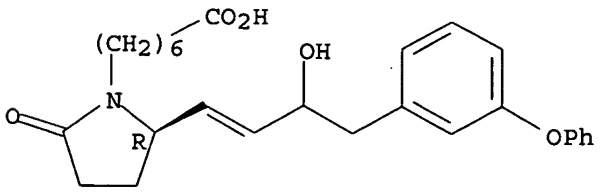
RN 346673-10-7 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-(3-phenoxyphenyl)butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



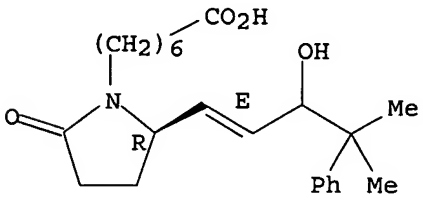
RN 431989-51-4 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[3-hydroxy-4-(3-phenoxyphenyl)-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



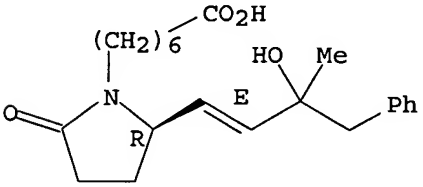
RN 540731-22-4 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E)-3-hydroxy-4-methyl-4-phenyl-1-pentenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



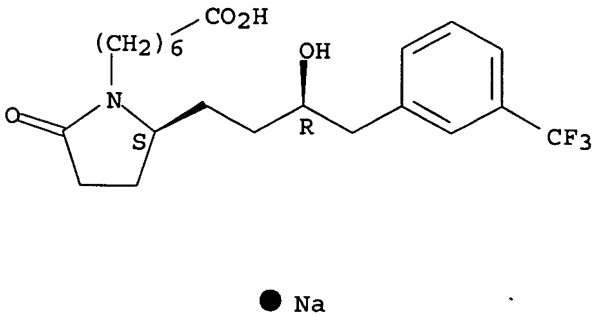
RN 540731-32-6 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E)-3-hydroxy-3-methyl-4-phenyl-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **346672-62-6P 346672-72-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(treatment of ocular hypertension by using potent and selective agonists of the EP4 subtype of prostaglandin E2 receptors)
RN 346672-62-6 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl]-5-oxo-, monosodium salt, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

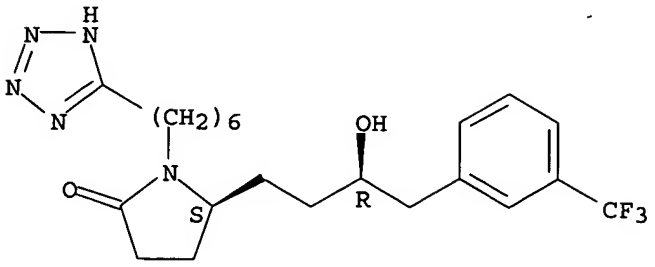


● Na

RN 346672-72-8 CAPLUS
CN 2-Pyrrolidinone, 5-[(3R)-3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, monosodium salt, (5S)- (9CI) (CA INDEX

NAME)

Absolute stereochemistry.



● Na

L9 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:429101 CAPLUS
DOCUMENT NUMBER: 139:982
TITLE: 8-Azaprostaglandin analogs as agents for lowering intraocular pressure
INVENTOR(S): Old, David W.; Dinh, Danny Thang; Burk, Robert M.
PATENT ASSIGNEE(S): Allergan, Inc., USA
SOURCE: U.S., 15 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6573294	B1	20030603	US 2002-146224	20020514
US 2003220506	A1	20031127	US 2003-411036	20030409
US 2004157912	A1	20040812	US 2003-470566	20030409
WO 2003097596	A1	20031127	WO 2003-US13300	20030428

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-146224 A1 20020514
OTHER SOURCE(S): MARPAT 139:982

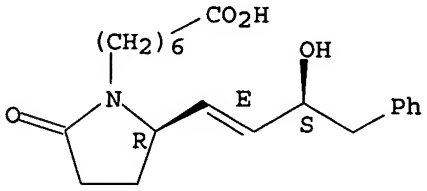
AB The present invention provides a method of treating ocular hypertension or glaucoma which comprises administering to an animal having ocular hypertension or glaucoma therapeutically effective amount of a 8-azaprostaglandin analog formulated as an ophthalmic solution and packaged in a container suitable for metered application.

IT **66598-57-0P 66598-64-9P 346672-57-9P 346672-61-5P 494221-70-4P 494221-79-3P**

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(azaprostaglandin analogs for lowering intraocular pressure)

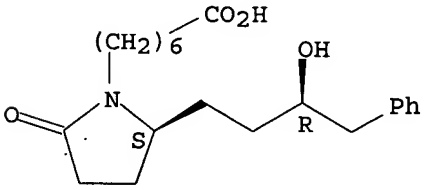
RN 66598-57-0 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



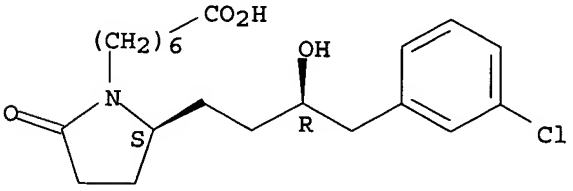
RN 66598-64-9 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-phenylbutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



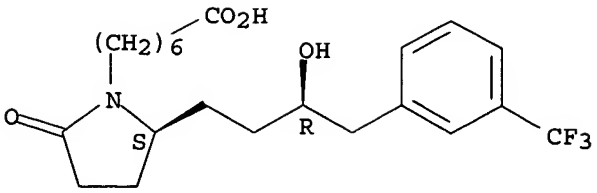
RN 346672-57-9 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-4-(3-chlorophenyl)-3-hydroxybutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



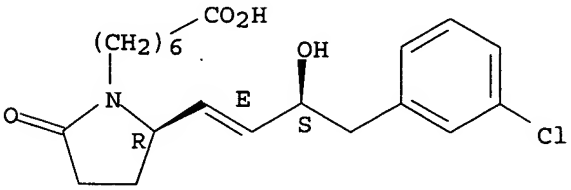
RN 346672-61-5 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



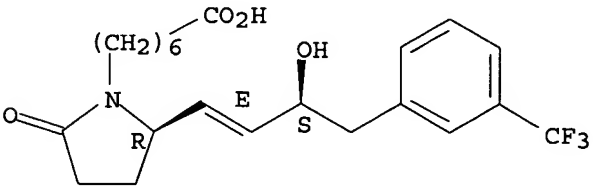
RN 494221-70-4 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-4-(3-chlorophenyl)-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 494221-79-3 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-[3-(trifluoromethyl)phenyl]-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

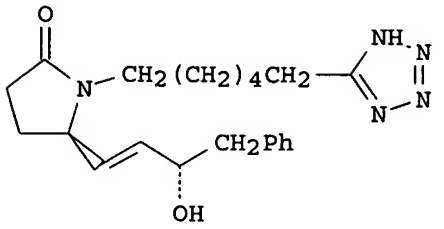
Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:215733 CAPLUS
DOCUMENT NUMBER: 139:100991
TITLE: Discovery of a potent and selective agonist of the prostaglandin EP4 receptor
AUTHOR(S): Billot, Xavier; Chateauneuf, Anne; Chauret, Nathalie; Denis, Danielle; Greig, Gillian; Mathieu, Marie-Claude; Metters, Kathleen M.; Slipetz, Deborah M.; Young, Robert N.
CORPORATE SOURCE: Merck Frosst Centre for Therapeutic Research, Pointe Claire-Dorval, QC, 1005, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(6), 1129-1132
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:100991
GI



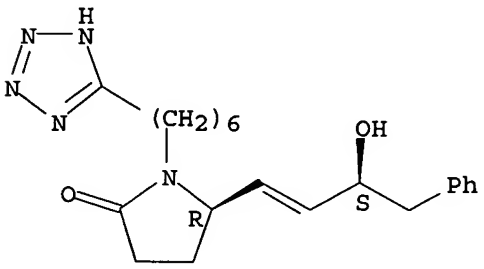
I

AB Analogs of PGE2, wherein the hydroxycyclopentanone ring has been replaced by a lactam, have been prepared and evaluated as ligands for the EP4 receptor. An optimized compound (I) shows high potency and agonist efficacy at the EP4 receptor and is highly selective over the other seven known prostaglandin receptors.

IT **346673-06-1P 557086-86-9P**
RL: BSU (Biological study, unclassified); PUR (Purification or recovery); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of PGE2 lactam analogs as potent and selective agonists of prostaglandin EP4 receptor)

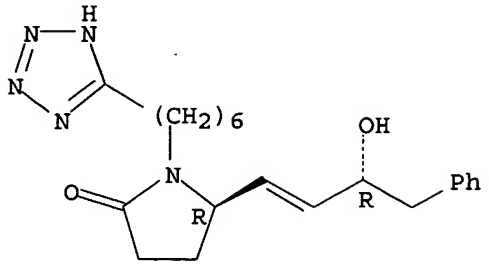
RN 346673-06-1 CAPLUS
CN 2-Pyrrolidinone, 5-[(3S)-3-hydroxy-4-phenyl-1-butenyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



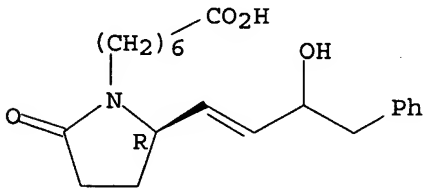
RN 557086-86-9 CAPLUS
CN 2-Pyrrolidinone, 5-[(3R)-3-hydroxy-4-phenyl-1-butenyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



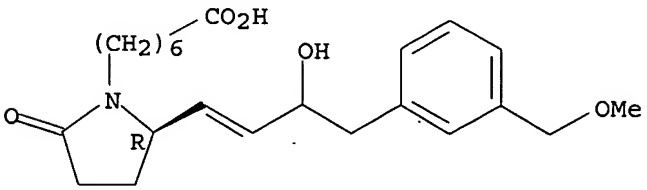
IT **557086-66-5P 557086-67-6P 557086-69-8P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of PGE2 lactam analogs as potent and selective agonists of prostaglandin EP4 receptor)
RN 557086-66-5 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-(3-hydroxy-4-phenyl-1-butenyl)-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



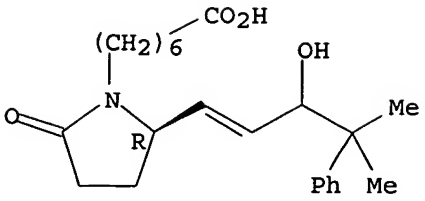
RN 557086-67-6 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[3-hydroxy-4-[3-(methoxymethyl)phenyl]-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 557086-69-8 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-(3-hydroxy-4-methyl-4-phenyl-1-pentenyl)-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:97322 CAPLUS
DOCUMENT NUMBER: 138:142493
TITLE: Remedies for diseases with bone mass loss having EP4 agonist as the active ingredient
INVENTOR(S): Maruyama, Toru; Kobayashi, Kaoru; Kambe, Tohru; Maruyama, Takayuki; Yoshida, Hideyuki; Nishiura, Akio; Abe, Nobutaka
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 474 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003009872	A1	20030206	WO 2002-JP7385	20020722
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1417975	A1	20040512	EP 2002-747707	20020722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011364	A	20040713	BR 2002-11364	20020722
PRIORITY APPLN. INFO.:			JP 2001-222148 A	20010723
			JP 2001-239895 A	20010807
			JP 2002-56449 A	20020301
			WO 2002-JP7385 W	20020722

OTHER SOURCE(S): MARPAT 138:142493

AB Disclosed are drugs for topical administration which contain an EP4 agonist as the active ingredient for preventing and/or treating diseases in association with bone mass loss. The EP4 agonists typified by compds. with the prostaglandin skeleton have an effect of promoting osteogenesis. Thus, topical administration thereof is highly useful in preventing and/or treating diseases in association with bone mass loss, e.g., bone diseases such as primary osteoporosis, secondary osteoporosis, bone metastasis of cancer, hypercalcemia, Behcet's disease, bone loss and bone necrosis, postoperative osteogenesis, alternative therapy for bone transplantation.

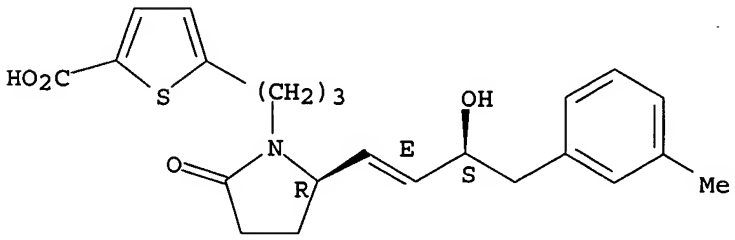
A compound (11α,15α,13E)-9-oxo-11,15-dihydroxy-16-(3-methoxymethylphenyl)-17,18,19,20-tetranor-5-thiaprost-13-enoic acid 2-nonanoyloxyethyl ester was prepared, and mixed with lactic acid-glycolic acid copolymer to obtain a microsphere. The obtained microsphere was administered to fracture bone part of a rat to examine the bone formation promoting effect.

IT **494222-13-8P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(remedies for diseases with bone mass loss containing prostaglandin EP4 receptor agonists as active ingredients)

RN 494222-13-8 CAPLUS

CN 2-Thiophenecarboxylic acid, 5-[3-[(2R)-2-[(1E,3S)-3-hydroxy-4-(3-methylphenyl)-1-butenyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

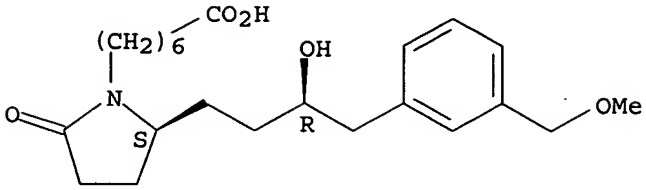


IT **431989-16-1P 494221-64-6P 494221-69-1P**
494221-70-4P 494221-71-5P 494221-72-6P
494221-73-7P 494221-74-8P 494221-75-9P
494221-76-0P 494221-77-1P 494221-78-2P
494221-79-3P 494221-80-6P 494221-81-7P
494221-82-8P 494221-83-9P 494221-84-0P
494221-85-1P 494221-86-2P 494221-87-3P
494221-88-4P 494221-89-5P 494221-90-8P
494221-91-9P 494221-92-0P 494221-93-1P
494221-94-2P 494221-95-3P 494221-96-4P
494221-97-5P 494221-98-6P 494221-99-7P
494222-03-6P 494222-04-7P 494222-06-9P
494222-14-9P 494222-15-0P 494222-17-2P
494222-18-3P 494222-87-6P 494223-74-4P
494223-75-5P 494223-78-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(remedies for diseases with bone mass loss containing prostaglandin EP4 receptor agonists as active ingredients)

RN 431989-16-1 CAPLUS

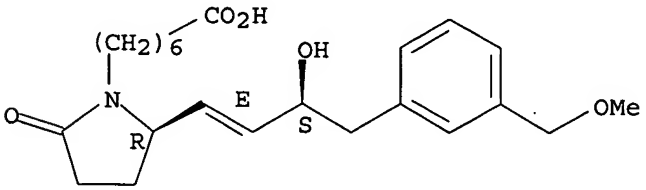
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-[3-(methoxymethyl)phenyl]butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



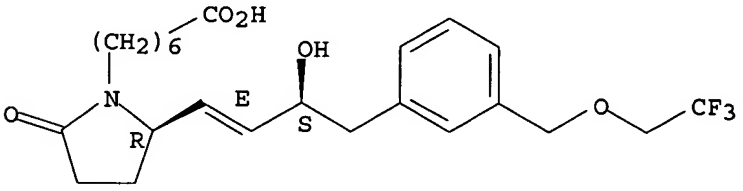
RN 494221-64-6 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-[3-(methoxymethyl)phenyl]-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



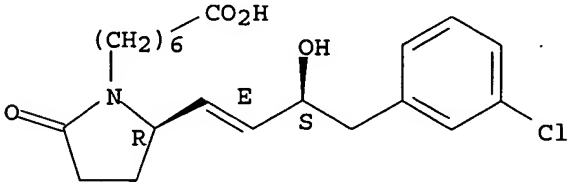
RN 494221-69-1 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-[3-[(2,2,2-trifluoroethoxy)methyl]phenyl]-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 494221-70-4 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-4-(3-chlorophenyl)-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

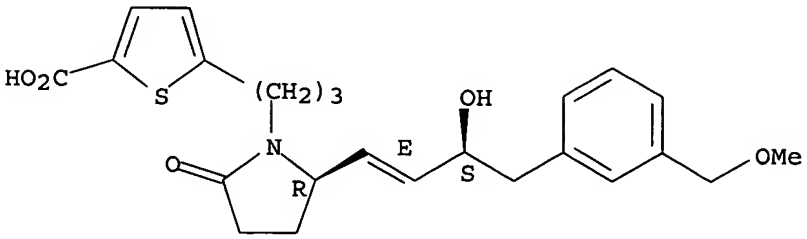
Absolute stereochemistry.
Double bond geometry as shown.



RN 494221-71-5 CAPLUS

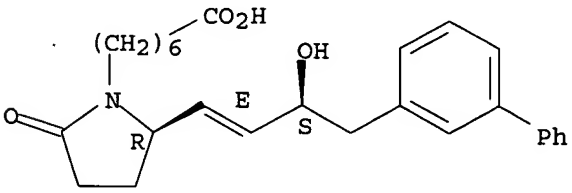
CN 2-Thiophenecarboxylic acid, 5-[3-[(2R)-2-[(1E,3S)-3-hydroxy-4-[3-(methoxymethyl)phenyl]-1-butenyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



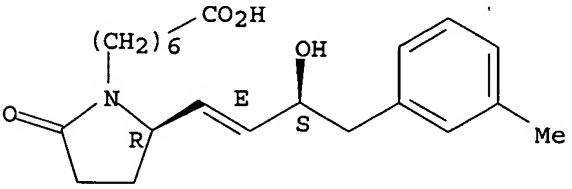
RN 494221-72-6 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-4-[1,1'-biphenyl]-3-yl-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



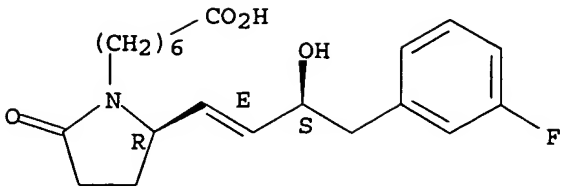
RN 494221-73-7 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-(3-methylphenyl)-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



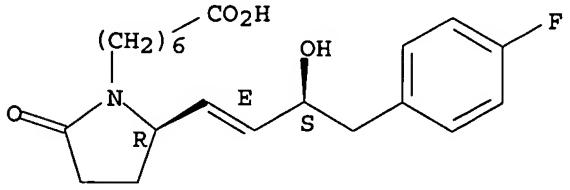
RN 494221-74-8 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-4-(3-fluorophenyl)-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



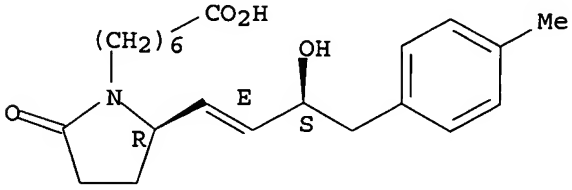
RN 494221-75-9 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



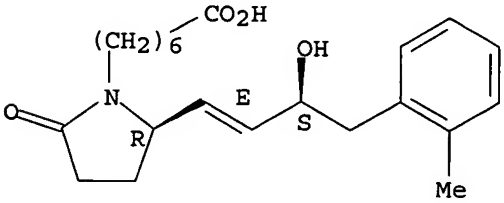
RN 494221-76-0 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-(4-methylphenyl)-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 494221-77-1 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-(2-methylphenyl)-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

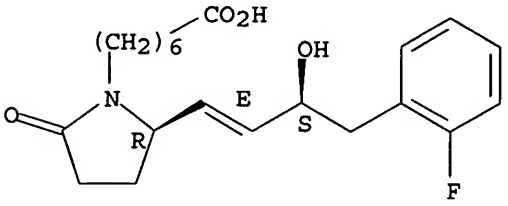
Absolute stereochemistry.
Double bond geometry as shown.



RN 494221-78-2 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-4-(2-fluorophenyl)-3-hydroxy-1-

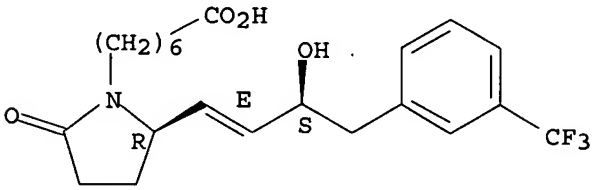
butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



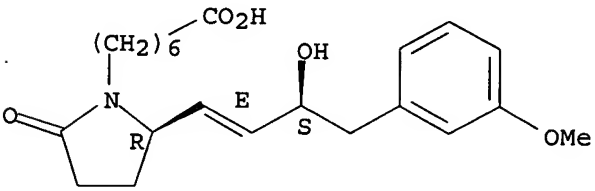
RN 494221-79-3 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-[3-(trifluoromethyl)phenyl]-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



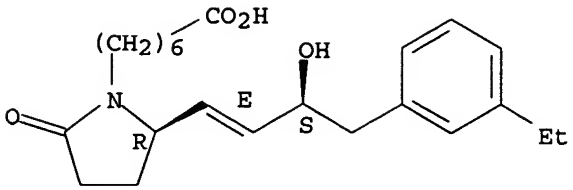
RN 494221-80-6 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-(3-methoxyphenyl)-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



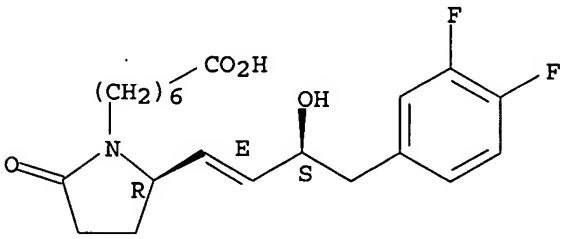
RN 494221-81-7 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-4-(3-ethylphenyl)-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



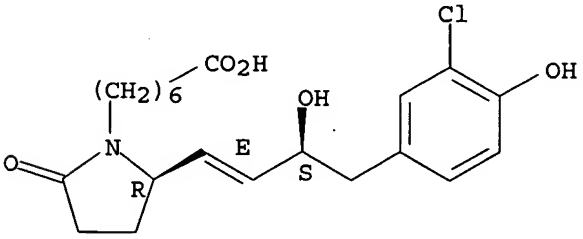
RN 494221-82-8 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-4-(3,4-difluorophenyl)-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



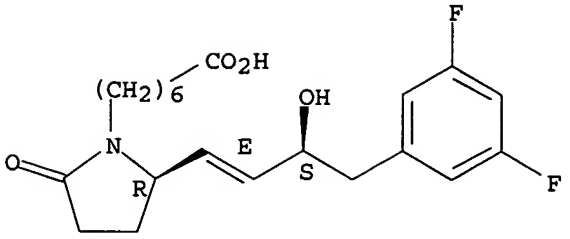
RN 494221-83-9 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-4-(3-chloro-4-hydroxyphenyl)-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



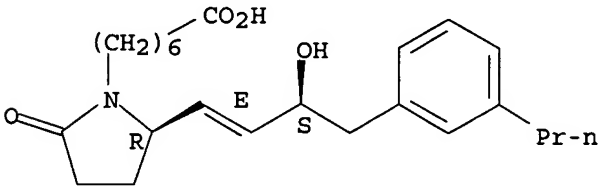
RN 494221-84-0 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-4-(3,5-difluorophenyl)-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



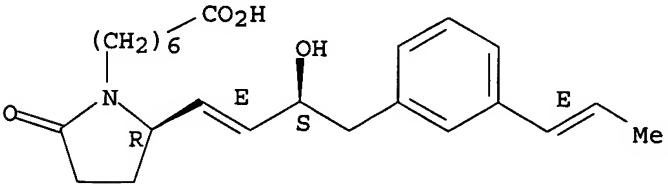
RN 494221-85-1 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-(3-propylphenyl)-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



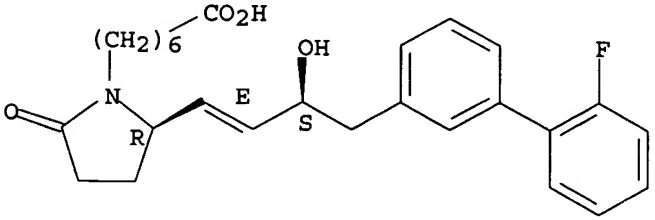
RN 494221-86-2 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-[3-(1E)-1-propenylphenyl]-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



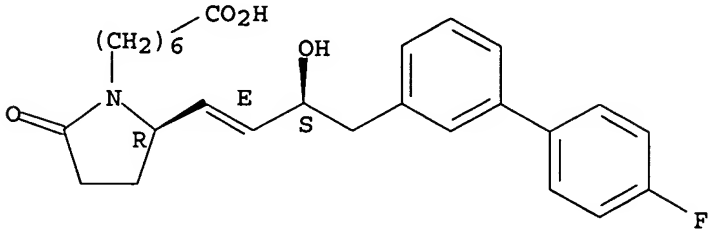
RN 494221-87-3 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-4-(2'-fluoro[1,1'-biphenyl]-3-yl)-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



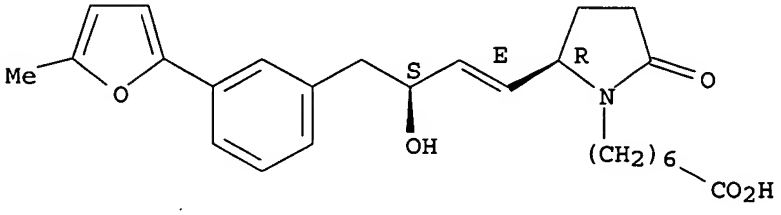
RN 494221-88-4 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-4-(4'-fluoro[1,1'-biphenyl]-3-yl)-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



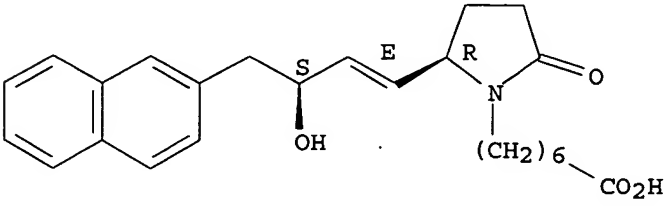
RN 494221-89-5 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-[3-(5-methyl-2-furanyl)phenyl]-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



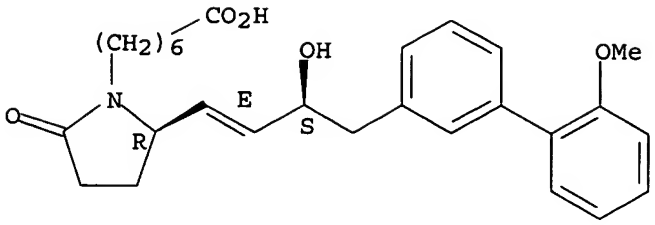
RN 494221-90-8 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-(2-naphthalenyl)-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



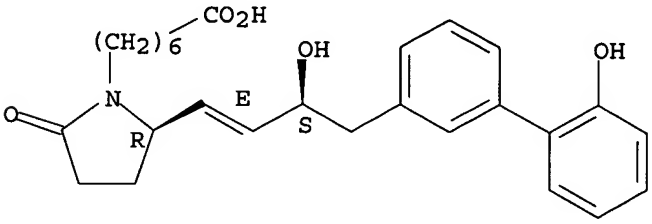
RN 494221-91-9 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-(2'-methoxy[1,1'-biphenyl]-3-yl)-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



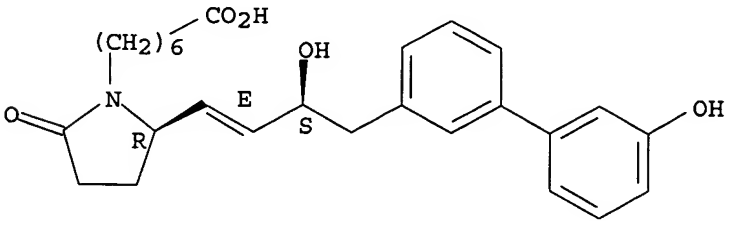
RN 494221-92-0 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-(2'-hydroxy[1,1'-biphenyl]-3-yl)-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



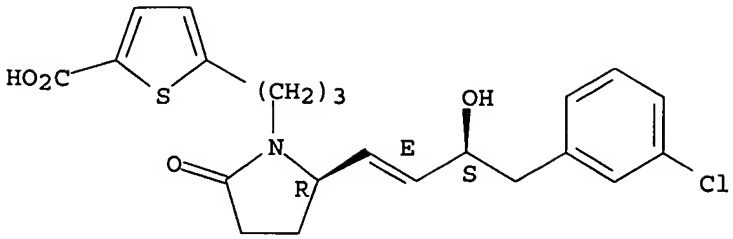
RN 494221-93-1 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-(3'-hydroxy[1,1'-biphenyl]-3-yl)-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



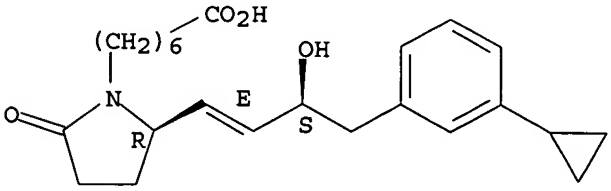
RN 494221-94-2 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2R)-2-[(1E,3S)-4-(3-chlorophenyl)-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



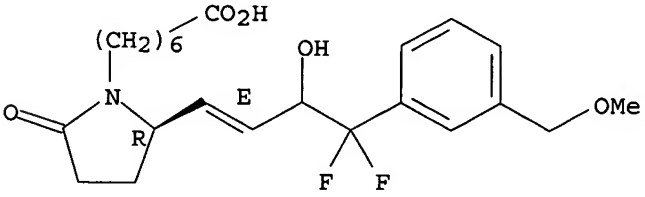
RN 494221-95-3 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-4-(3-cyclopropylphenyl)-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



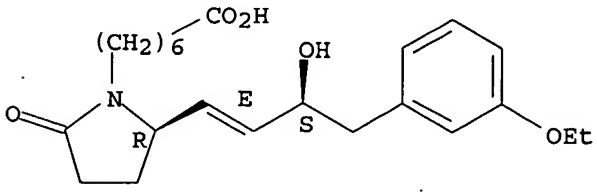
RN 494221-96-4 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E)-4,4-difluoro-3-hydroxy-4-[3-(methoxymethyl)phenyl]-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 494221-97-5 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-4-(3-ethoxyphenyl)-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

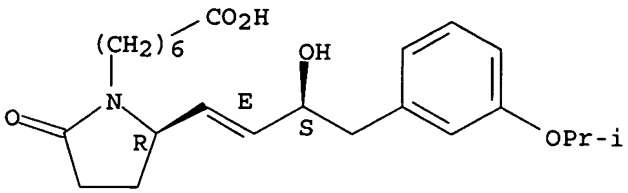
Absolute stereochemistry.
Double bond geometry as shown.



RN 494221-98-6 CAPLUS

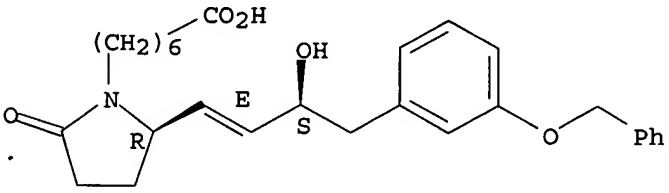
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-[3-(1-methylethoxy)phenyl]-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



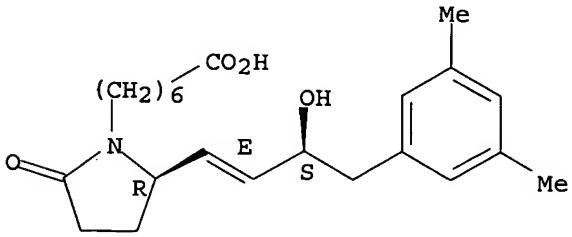
RN 494221-99-7 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-[3-(phenylmethoxy)phenyl]-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



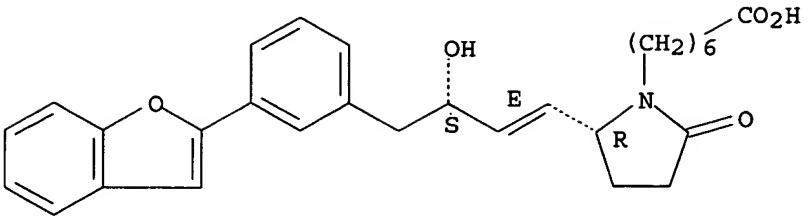
RN 494222-03-6 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-4-(3,5-dimethylphenyl)-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



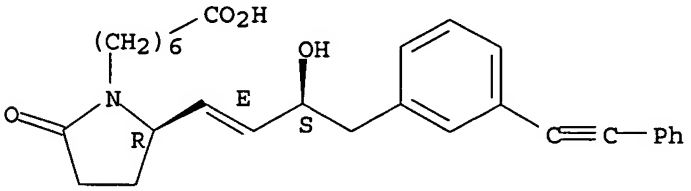
RN 494222-04-7 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-4-[3-(2-benzofuranyl)phenyl]-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



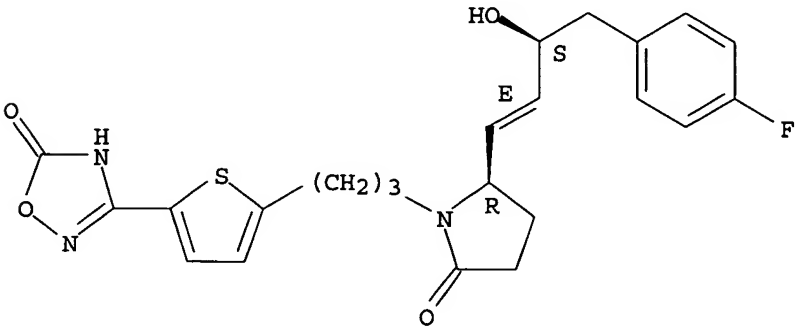
RN 494222-06-9 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-[3-(phenylethynyl)phenyl]-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



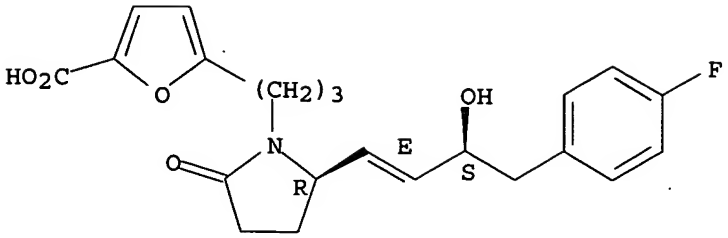
RN 494222-14-9 CAPLUS
CN 1,2,4-Oxadiazol-5(2H)-one, 3-[5-[3-[(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]propyl]-2-thienyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



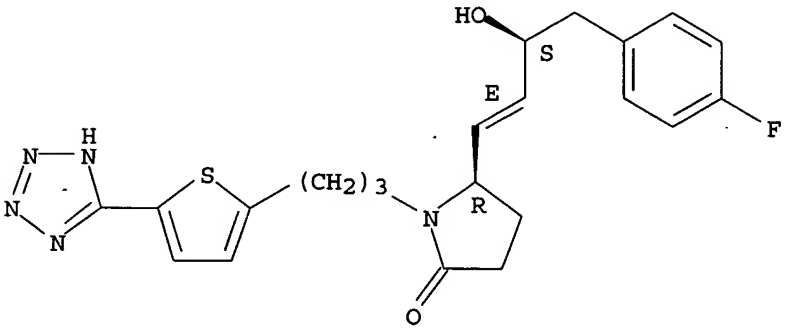
RN 494222-15-0 CAPLUS
CN 2-Furancarboxylic acid, 5-[3-[(2R)-2-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



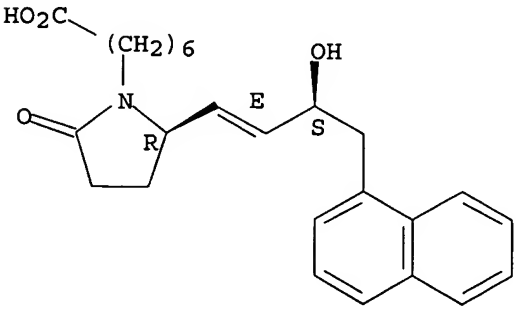
RN 494222-17-2 CAPLUS
CN 2-Pyrrolidinone, 5-[(1E,3S)-4-(4-fluorophenyl)-3-hydroxy-1-butenyl]-1-[3-[5-(1H-tetrazol-5-yl)-2-thienyl]propyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



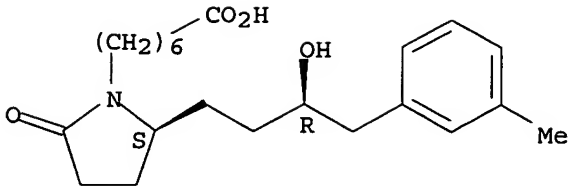
RN 494222-18-3 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-(1-naphthalenyl)-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



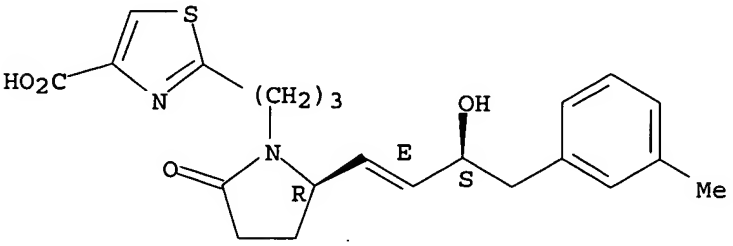
RN 494222-87-6 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-(3-methylphenyl)butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



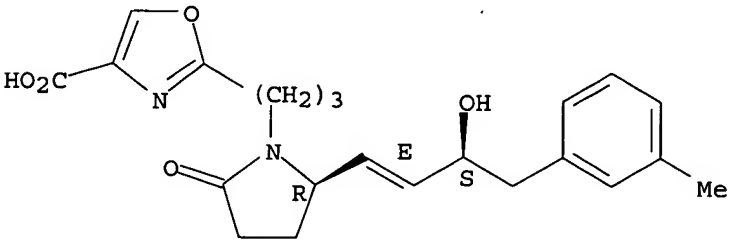
RN 494223-74-4 CAPLUS
CN 4-Thiazolecarboxylic acid, 2-[3-[(2R)-2-[(1E,3S)-3-hydroxy-4-(3-methylphenyl)-1-butenyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



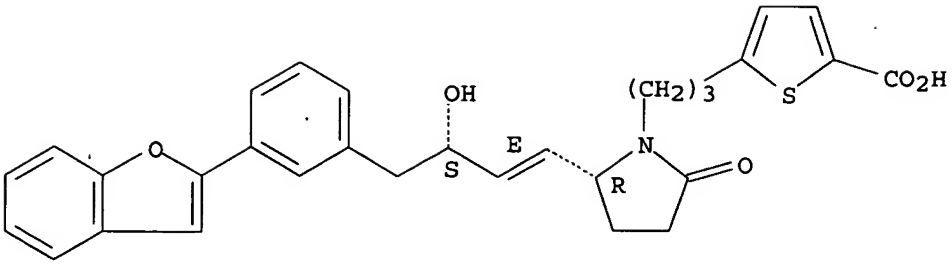
RN 494223-75-5 CAPLUS
CN 4-Oxazolecarboxylic acid, 2-[3-[(2R)-2-[(1E,3S)-3-hydroxy-4-(3-methylphenyl)-1-butenyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 494223-78-8 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2R)-2-[(1E,3S)-4-[3-(2-benzofuranyl)phenyl]-3-hydroxy-1-butenyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



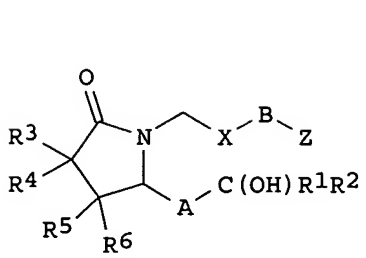
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:76747 CAPLUS
DOCUMENT NUMBER: 138:137086
TITLE: Preparation of pyrrolidine prostaglandin analogs for therapeutic use as EP4-type prostanoid receptor agonists
INVENTOR(S): Elworthy, Todd Richard; Mirzadegan, Taraneh; Roepel, Michael Garret; Smith, David Bernard; Walker, Keith Adrian Murray
PATENT ASSIGNEE(S): F. Hoffmann-La Roche AG, Switz.
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008377	A1	20030130	WO 2002-EP7574	20020708
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1409455	A1	20040421	EP 2002-764647	20020708
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011201	A	20040713	BR 2002-11201	20020708
JP 2004521954	T2	20040722	JP 2003-513937	20020708
US 2003120079	A1	20030626	US 2002-197353	20020716

PRIORITY APPLN. INFO.:	US 2001-305727P	P	20010716
	US 2002-371348P	P	20020410
	WO 2002-EP7574	W	20020708

OTHER SOURCE(S): MARPAT 138:137086
GI



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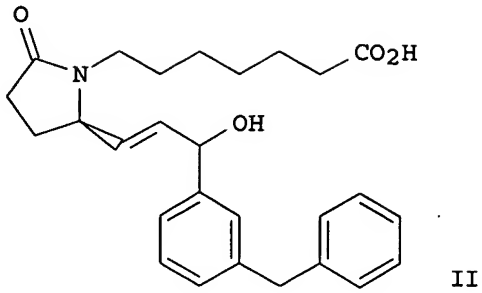
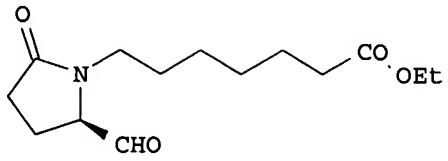


II



III

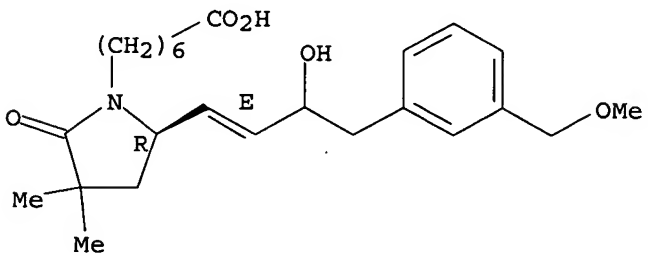
AB 8-Aza prostanoid analogs, such as I [R1 = alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl; R2-6 = H, alkyl, alkenyl, alkynyl; A = CH2CH2, CH:CH, CH:CHCH2; B = bond, aryl, heteroaryl; X = (CH2)1-6; Z = CH2OH, CO2H, tetrazol-5-yl, carboxy, carboxamido, phosphonate, etc.], were prepared as selective EP4-type prostanoid receptor agonists for pharmaceutical use in the treatment of bone disorders. Thus, azaprostanoid II was via a series of synthetic steps which included an olefination reaction of ester III with (MeO)2P(O)CH2COC6H4-3-CH2Ph. The prepared azaprostanoids were assayed for competitive binding of [3H]PGE2 to prostanoid types EP1, EP2, EP3, and EP4 receptors. Also, pharmaceutical formulations of the azaprostanoids were presented.

IT **493036-07-0P 493036-37-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidine prostaglandin analogs for therapeutic use as EP4 prostanoid receptor agonists for treatment of bone disorders)

RN 493036-07-0 CAPLUS

CN 1-Pyrrolidineheptanoic acid, 5-[(1E)-3-hydroxy-4-[3-(methoxymethyl)phenyl]-1-butenyl]-3,3-dimethyl-2-oxo-, (5R)- (9CI) (CA INDEX NAME)

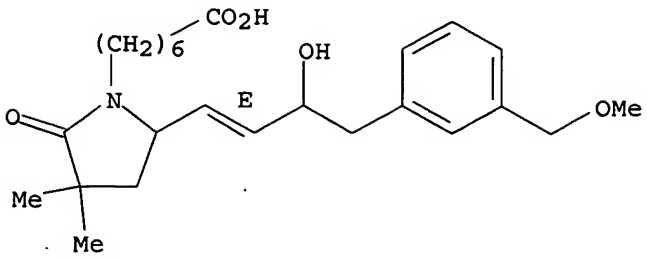
Absolute stereochemistry.
Double bond geometry as shown.



RN 493036-37-6 CAPLUS

CN 1-Pyrrolidineheptanoic acid, 5-[(1E)-3-hydroxy-4-[3-(methoxymethyl)phenyl]-1-butenyl]-3,3-dimethyl-2-oxo- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:408643 CAPLUS
DOCUMENT NUMBER: 137:6083
TITLE: Preparation of EP4 receptor selective agonists for the treatment of osteoporosis
INVENTOR(S): Cameron, Kimberly O'Keefe; Lefker, Bruce Allen
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002042268	A2	20020530	WO 2001-IB2073		20011105
WO 2002042268	A3	20020725			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2429850	AA	20020530	CA 2001-2429850		20011105
AU 2002010848	A5	20020603	AU 2002-10848		20011105
EP 1339678	A2	20030903	EP 2001-978757		20011105
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BR 2001015687	A	20030909	BR 2001-15687		20011105
EE 200300246	A	20031015	EE 2003-246		20011105
JP 2004521869	T2	20040722	JP 2002-544404		20011105
US 20020065308	A1	20020530	US 2001-990556		20011121
US 6552067	B2	20030422			
US 2003149086	A1	20030807	US 2002-326366		20021220
US 6747054	B2	20040608			
BG 107697	A	20040130	BG 2003-107697		20030403
ZA 2003002803	A	20040413	ZA 2003-2803		20030410
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US 2004259921	A1	20041223	US 2003-668633		20030923
PRIORITY APPLN. INFO.:			US 2000-253275P	P	20001127
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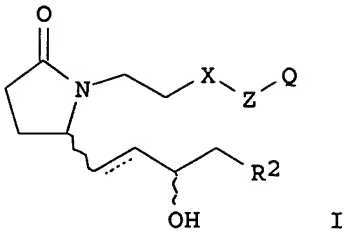
US 2001-990556 A3 20011121
US 2002-326366 A3 20021220

OTHER SOURCE(S): MARPAT 137:6083

GI



I

AB This invention is directed to EP4 receptor selective prostaglandin agonists I (e.g. 4-[3-[2-(3-hydroxy-4-phenylbutyl)-5-oxopyrrolidin-1-yl]propyl]benzoic acid), wherein R2, X, Z and Q are defined below and in more detail in the claims. This invention is also directed to pharmaceutical compns. containing those compds. This invention is also directed to methods of treating conditions which present with low bone mass, particularly osteoporosis, frailty, an osteoporotic fracture, a bone defect, childhood idiopathic bone loss, alveolar bone loss, mandibular bone loss, bone fracture, osteotomy, bone loss associated with periodontitis, or prosthetic ingrowth in a mammal comprising administering those compds. Although biol. testing protocols are included, no test results are given. In I, a prodrug thereof, a pharmaceutically acceptable salt of said compound or said prodrug or a stereoisomer or diastereomeric mixture of said compound, prodrug or salt: the dotted line is a bond or no bond; X is -CH2- or O; Z is -(CH2)3-, thienyl, thiazolyl or Ph, provided that when X is O, then Z is phenyl; Q is carboxy, (C1-C4)alkoxycarbonyl or tetrazolyl; R2 is -Ar or -Ar1-V-Ar2; V is a bond, -O-, -OCH2- or -CH2O-. Ar is a partially saturated, fully saturated or fully unsatd. 5-8 membered ring optionally having 1-4 heteroatoms selected independently from O, S and N, or a bicyclic ring consisting of two fused independently partially saturated, fully saturated or fully unsatd. 5-6 membered rings, taken independently, optionally having 1-4 heteroatoms selected independently from N, S and O, said partially or fully saturated ring or bicyclic ring optionally having 1-2 oxo groups substituted on C or 1-2 oxo groups substituted on S. Ar1 and Ar2 are each independently a partially saturated, fully saturated or fully unsatd. 5-8 membered ring optionally having 1-4 heteroatoms selected independently from O, S and N, said partially or fully saturated ring optionally having 1-2 oxo groups substituted on C or 1-2 oxo groups substituted on S. Ar is optionally substituted on C or N, on one ring if the moiety is monocyclic, or on one or both rings if the moiety is bicyclic, with up to three substituents per ring each independently selected from hydroxy, halo, carboxy, (C1-C7) alkoxy, (C1-C4)alkoxy(C1-C4)alkyl, (C1-C7)alkyl, (C2-C7)alkenyl, (C3-C7)cycloalkyl, (C3-C7)cycloalkyl(C1-C4)alkyl, (C3-C7)cycloalkyl(C1-C4)alkanoyl, formyl, (C1-C8) alkanoyl, (C1-C6)alkanoyl(C1-C6)alkyl, (C1-C4)alkanoylamino, (C1-C4)alkoxycarbonylamino, hydroxysulfonyl, aminocarbonylamino or mono-N-, di-N,N-, di-N,N'- or tri-N,N,N'-(C1-C4)alkyl substituted aminocarbonylamino, sulfonamido, (C1-C4)alkylsulfonamido, amino, mono-N- or di-N,N-(C1-C4)alkylamino, carbamoyl, mono-N- or di-N,N-(C1-C4)alkylcarbamoyl, cyano, thiol, (C1-C6)alkylthio, (C1-C6)alkylsulfinyl, (C1-C4)alkylsulfonyl and mono-N- or di-N,N-(C1-C4)alkylaminosulfinyl, wherein said alkyl and alkoxy substituents in the definition of Ar are optionally substituted on C with

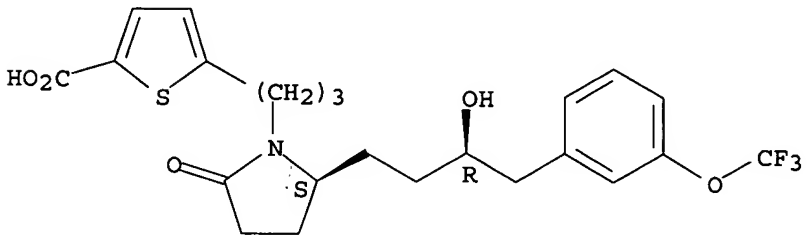
up to three fluoro. Ar1 and Ar2 are independently optionally substituted on C or N with up to three substituents each independently selected from hydroxy, halo, carboxy, (C1-C7)alkoxy, (C1-C4)alkoxy(C1-C4)alkyl, (C1-C7)alkyl, (C2-C7)alkenyl, (C3-C7)cycloalkyl, (C3-C7)cycloalkyl(C1-C4)alkyl, (C3-C7)cycloalkyl(C1-C4)alkanoyl, formyl, (C1-C8)alkanoyl, (C1-C6)alkanoyl(C1-C6)alkyl, (C1-C4)alkanoylamino, (C1-C4)alkoxycarbonylamino, hydroxysulfonyl, aminocarbonylamino or mono-N-, di-N,N-, di-N,N'- or tri-N,N,N'-(C1-C4)alkyl substituted aminocarbonylamino, sulfonamido, (C1-C4)alkylsulfonamido, amino, mono-N- or di-N,N-(C1-C4)alkylamino, carbamoyl, mono-N- or di-N,N-(C1-C4)alkylcarbamoyl, cyano, thiol, (C1-C6)alkylthio, (C1-C6)alkylsulfinyl, (C1-C4)alkylsulfonyl and mono-N- or di-N,N-(C1-C4)alkylaminosulfinyl, wherein said alkyl and alkoxy substituents in the definition of Ar1 and Ar2 are optionally substituted on C with up to three fluoro. (a) when X is (CH2)- and Z is -(CH2)3-, then R2 is not thienyl, Ph or Ph monosubstituted with chloro, fluoro, Ph, methoxy, trifluoromethyl or (C1-C4) alkyl; and (b) when X is (CH2)-, Z is -(CH2)3-, and Q is carboxy or (C1-C4) alkoxycarbonyl, then R2 is not (i) (C5-C7)cycloalkyl or (ii)phenyl, thienyl or furyl each of which may be optionally monosubstituted or disubstituted by one or two substituents selected, independently in the latter case, from halogen atoms, alkyl groups having 1-3 C atoms which may be substituted by one or more halogen atoms, and alkoxy groups having 1-4 C atoms. Although the methods of preparation are not claimed, 41 example prepns. are included.

IT **431991-28-5**, 5-[3-[(2S)-[(3R)-Hydroxy-4-(3-trifluoromethoxyphenyl)butyl]-5-oxopyrrolidin-1-yl]propyl]thiophene-2-carboxylic acid
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(EP4 receptor selective agonist for treatment of osteoporosis)

RN 431991-28-5 CAPLUS

CN 2-Thiophenecarboxylic acid, 5-[3-[(2S)-2-[(3R)-3-hydroxy-4-[3-(trifluoromethoxy)phenyl]butyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

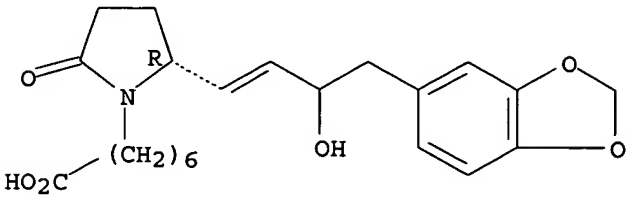


IT **431989-27-4P**, 7-[2R-(4-Benzo[1,3]dioxol-5-yl-3-hydroxybut-1-enyl)-5-oxopyrrolidin-1-yl]heptanoic acid **431989-84-3P**, 5-[3-[(2S)-[4-(3-Fluorophenyl)-3-hydroxybutyl]-5-oxopyrrolidin-1-yl]propyl]thiophene-2-carboxylic acid **431990-16-8P**, (5S)-[(3R)-Hydroxy-4-(3-methoxymethylphenyl)butyl]-1-[6-(2H-tetrazol-5-yl)hexyl]pyrrolidin-2-one **431990-21-5P**, 2-[3-[(2S)-(3-Hydroxy-4-phenylbutyl)-5-oxopyrrolidin-1-yl]propyl]thiazole-4-carboxylic acid
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(intermediate; preparation of EP4 receptor selective agonists for treatment of osteoporosis)

RN 431989-27-4 CAPLUS

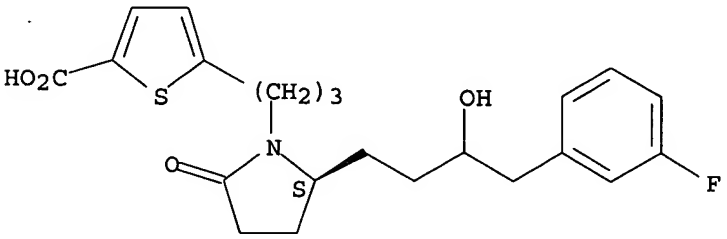
CN 1-Pyrrolidineheptanoic acid, 2-[4-(1,3-benzodioxol-5-yl)-3-hydroxy-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



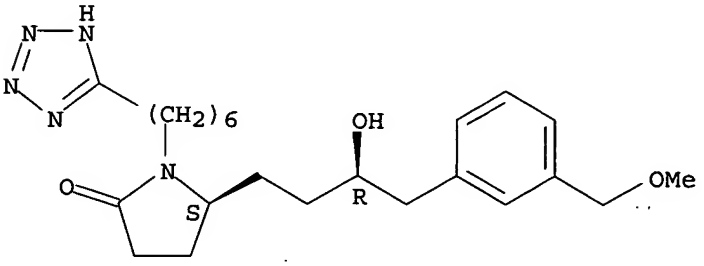
RN 431989-84-3 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2S)-2-[4-(3-fluorophenyl)-3-hydroxybutyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



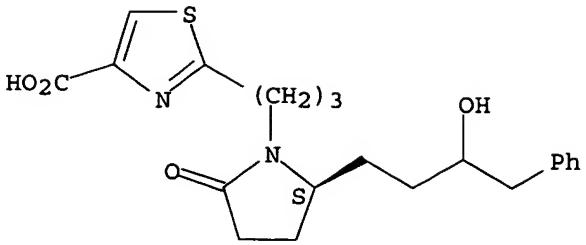
RN 431990-16-8 CAPLUS
CN 2-Pyrrolidinone, 5-[(3R)-3-hydroxy-4-[3-(methoxymethyl)phenyl]butyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



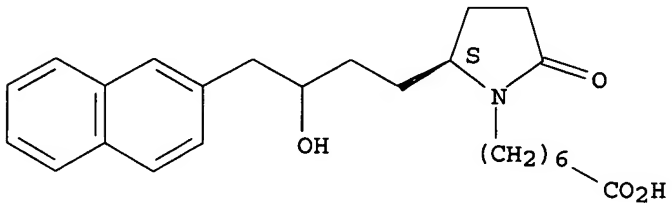
RN 431990-21-5 CAPLUS
CN 4-Thiazolecarboxylic acid, 2-[3-[(2S)-2-(3-hydroxy-4-phenylbutyl)-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



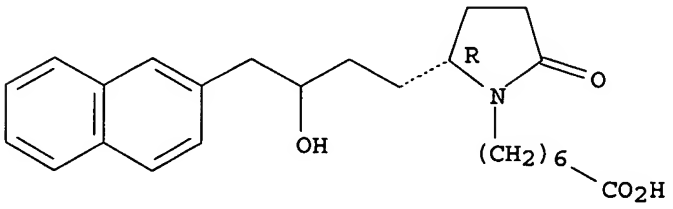
IT **431989-25-2P**, 7-[2S-(3-Hydroxy-4-naphthalen-2-ylbutyl)-5-oxopyrrolidin-1-yl]heptanoic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of EP4 receptor selective agonists for treatment of osteoporosis)
RN 431989-25-2 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[3-hydroxy-4-(2-naphthalenyl)butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **431989-21-8P**, 7-[2R-(3-Hydroxy-4-naphthalen-2-ylbutyl)-5-oxopyrrolidin-1-yl]heptanoic acid
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of EP4 receptor selective agonists for treatment of osteoporosis)
RN 431989-21-8 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[3-hydroxy-4-(2-naphthalenyl)butyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



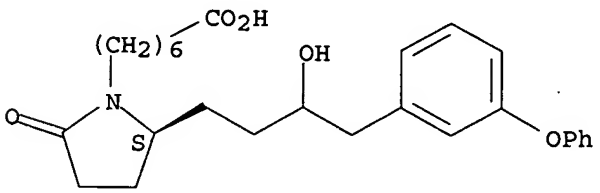
IT **346672-93-3P**, 7-[2S-[3-Hydroxy-4-(3-phenoxyphenyl)butyl]-5-oxopyrrolidin-1-yl]heptanoic acid **346673-09-4P**, 7-[2S-[3R-Hydroxy-4-(3-trifluoromethoxyphenyl)butyl]-5-oxopyrrolidin-1-yl]heptanoic acid **431989-16-1P**, 7-[2S-[3R-Hydroxy-4-(3-methoxymethylphenyl)butyl]-5-oxopyrrolidin-1-yl]heptanoic acid

431989-26-3P, Sodium salt of 7-[2S-(3-hydroxy-4-naphthalen-2-ylbutyl)-5-oxopyrrolidin-1-yl]heptanoic acid **431989-29-6P**, Sodium salt of 7-[2R-(4-Benzo[1,3]dioxol-5-yl-3-hydroxybut-1-enyl)-5-oxopyrrolidin-1-yl]heptanoic acid **431989-30-9P**, 7-[2S-(4-Benzo[1,3]dioxol-5-yl-3-hydroxybutyl)-5-oxopyrrolidin-1-yl]heptanoic acid **431989-40-1P**, 7-[2S-[4-(3-Cyanophenyl)-3R-hydroxybutyl]-5-oxopyrrolidin-1-yl]heptanoic acid **431989-46-7P**, 7-[2S-[3R-Hydroxy-4-[3-(2-methoxyethyl)phenyl]butyl]-5-oxopyrrolidin-1-yl]heptanoic acid **431989-51-4P**, 7-[2R-[3-Hydroxy-4-(3-phenoxyphenyl)but-1-enyl]-5-oxopyrrolidin-1-yl]heptanoic acid **431989-52-5P**, 5-[3-[2S-(3-Hydroxy-4-thiophen-2-ylbutyl)-5-oxopyrrolidin-1-yl]propyl]thiophene-2-carboxylic acid **431989-58-1P**, 5-[3-[2S-[4-(4-Chlorophenyl)-3-hydroxybutyl]-5-oxopyrrolidin-1-yl]propyl]thiophene-2-carboxylic acid **431989-62-7P**, 5-[3-[2S-[3-Hydroxy-4-(2-trifluoromethylphenyl)butyl]-5-oxopyrrolidin-1-yl]propyl]thiophene-2-carboxylic acid **431989-67-2P**, 5-[3-[2S-[4-(4-Fluorophenyl)-3-hydroxybutyl]-5-oxopyrrolidin-1-yl]propyl]thiophene-2-carboxylic acid **431989-71-8P**, 5-[3-[2S-[4-(4-Fluorophenyl)-3R-hydroxybutyl]-5-oxopyrrolidin-1-yl]propyl]thiophene-2-carboxylic acid **431989-74-1P**, 5-[3-[(2S)-(3-Hydroxy-4-naphthalen-2-ylbutyl)-5-oxopyrrolidin-1-yl]propyl]thiophene-2-carboxylic acid **431989-79-6P**, 5-[3-[(2S)-(4-(Biphenyl-3-yl)-3-hydroxybutyl)-5-oxopyrrolidin-1-yl]propyl]thiophene-2-carboxylic acid **431989-89-8P**, Sodium salt of 5-[3-[(2S)-[4-(3-Fluorophenyl)-3-hydroxybutyl]-5-oxopyrrolidin-1-yl]propyl]thiophene-2-carboxylic acid **431989-90-1P**, 5-[3-[(2S)-[4-(4-Ethylphenyl)-3-hydroxybutyl]-5-oxopyrrolidin-1-yl]propyl]thiophene-2-carboxylic acid **431989-95-6P**, 5-[3-[(2S)-[4-(4-Fluoro-3-methylphenyl)-3-hydroxybutyl]-5-oxopyrrolidin-1-yl]propyl]thiophene-2-carboxylic acid **431990-00-0P**, 5-[3-[(2S)-(3-Hydroxy-4-phenylbutyl)-5-oxopyrrolidin-1-yl]propyl]thiophene-2-carboxylic acid **431990-04-4P**, 5-[3-[(2S)-[4-(3-Chlorophenyl)-(3R)-hydroxybutyl]-5-oxopyrrolidin-1-yl]propyl]thiophene-2-carboxylic acid **431990-08-8P**, 5-[3-[(2S)-[(3R)-Hydroxy-4-(3-trifluoromethylphenyl)butyl]-5-oxopyrrolidin-1-yl]propyl]thiophene-2-carboxylic acid **431990-12-4P**, (5S)-(3-Hydroxy-4-(naphthalen-2-yl)butyl)-1-[6-(2H-tetrazol-5-yl)hexyl]pyrrolidin-2-one **431990-20-4P**, Sodium salt of (5S)-[(3R)-Hydroxy-4-(3-methoxymethylphenyl)butyl]-1-[6-(2H-tetrazol-5-yl)hexyl]pyrrolidin-2-one **431990-27-1P**, Sodium salt of 2-[3-[(2S)-(3-hydroxy-4-phenylbutyl)-5-oxopyrrolidin-1-yl]propyl]thiazole-4-carboxylic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of EP4 receptor selective agonists for treatment of osteoporosis)

RN 346672-93-3 CAPLUS

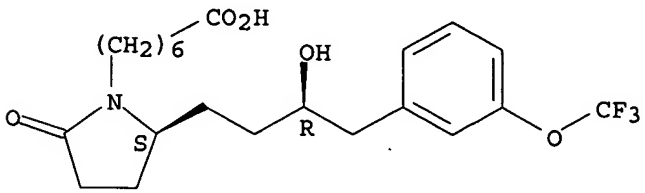
CN 1-Pyrrolidineheptanoic acid, 2-[3-hydroxy-4-(3-phenoxyphenyl)butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



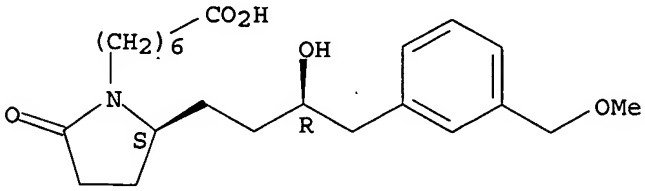
RN 346673-09-4 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-[3-(trifluoromethoxy)phenyl]butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



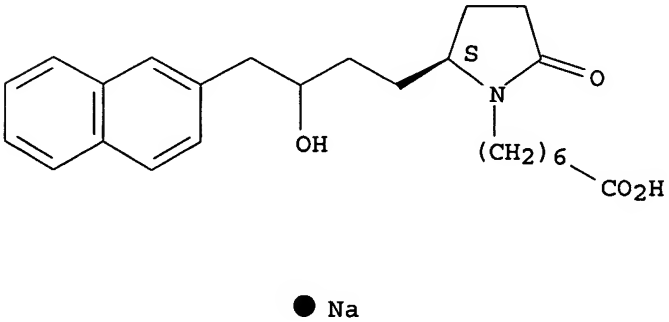
RN 431989-16-1 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-[3-(methoxymethyl)phenyl]butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 431989-26-3 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[3-hydroxy-4-(2-naphthalenyl)butyl]-5-oxo-, monosodium salt, (2S)- (9CI) (CA INDEX NAME)

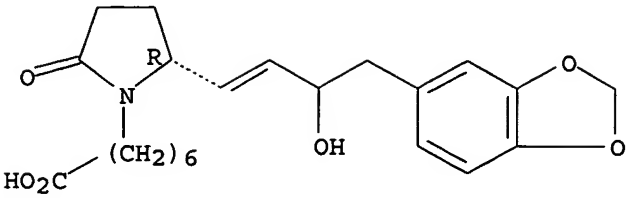
Absolute stereochemistry.



● Na

RN 431989-29-6 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[4-(1,3-benzodioxol-5-yl)-3-hydroxy-1-butenyl]-5-oxo-, monosodium salt, (2R)- (9CI) (CA INDEX NAME)

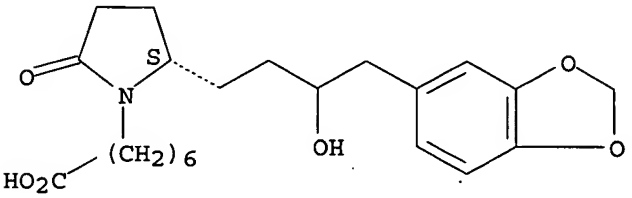
Absolute stereochemistry.
Double bond geometry unknown.



● Na

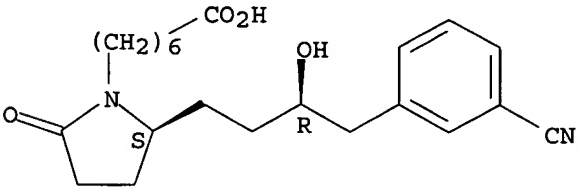
RN 431989-30-9 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[4-(1,3-benzodioxol-5-yl)-3-hydroxybutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



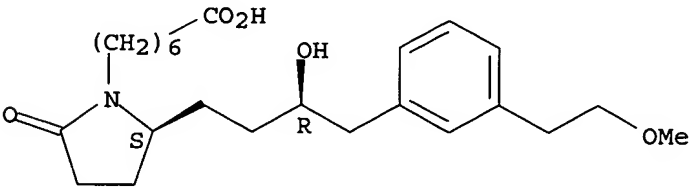
RN 431989-40-1 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-4-(3-cyanophenyl)-3-hydroxybutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 431989-46-7 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-[3-(2-methoxyethyl)phenyl]butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

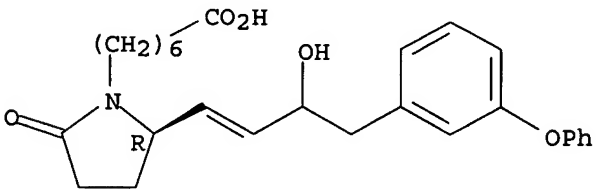
Absolute stereochemistry.



RN 431989-51-4 CAPLUS

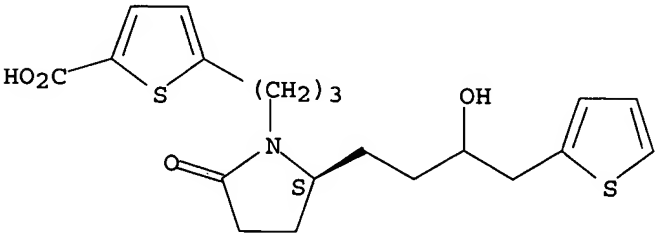
CN 1-Pyrrolidineheptanoic acid, 2-[3-hydroxy-4-(3-phenoxyphenyl)-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



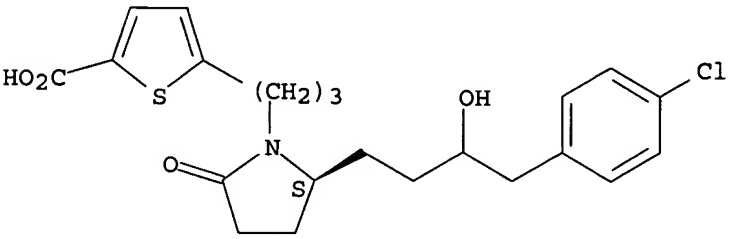
RN 431989-52-5 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2S)-2-[3-hydroxy-4-(2-thienyl)butyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



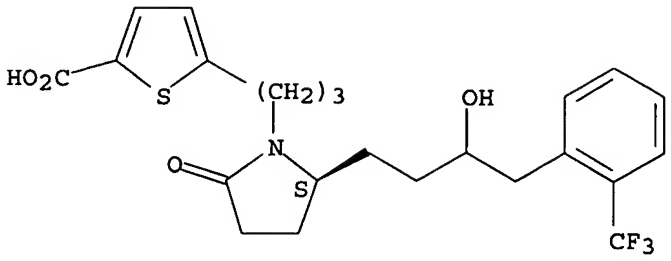
RN 431989-58-1 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2S)-2-[4-(4-chlorophenyl)-3-hydroxybutyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



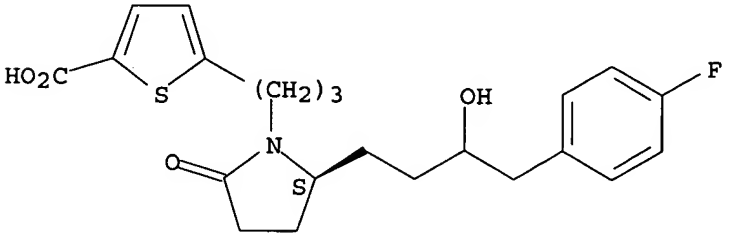
RN 431989-62-7 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2S)-2-[3-hydroxy-4-[2-(trifluoromethyl)phenyl]butyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



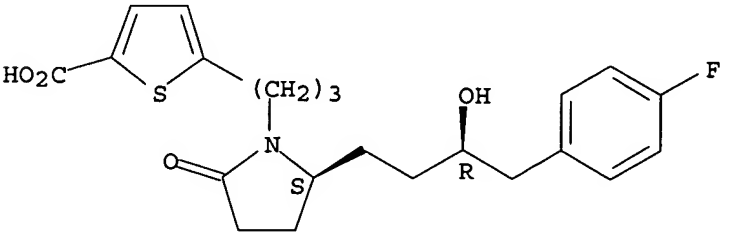
RN 431989-67-2 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2S)-2-[4-(4-fluorophenyl)-3-hydroxybutyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



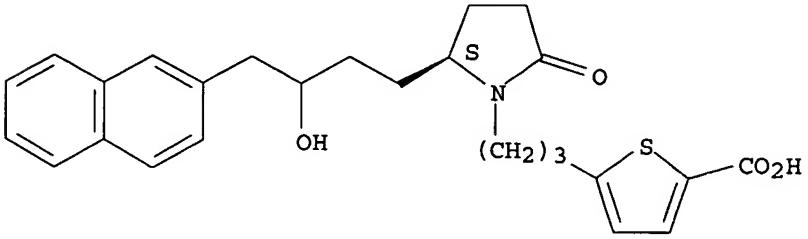
RN 431989-71-8 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2S)-2-[(3R)-4-(4-fluorophenyl)-3-hydroxybutyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



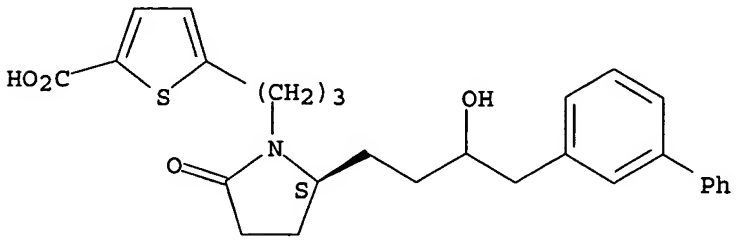
RN 431989-74-1 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2S)-2-[3-hydroxy-4-(2-naphthalenyl)butyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



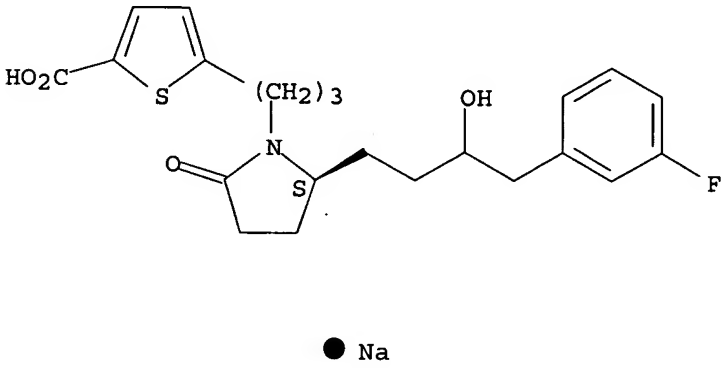
RN 431989-79-6 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2S)-2-(4-[1,1'-biphenyl]-3-yl-3-hydroxybutyl)-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



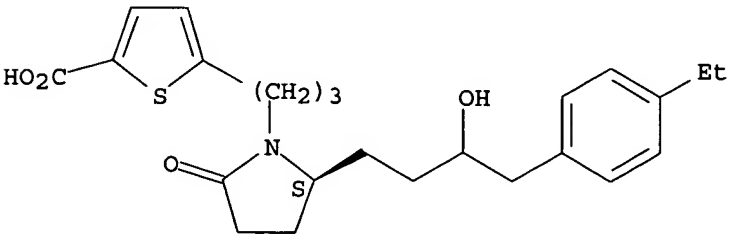
RN 431989-89-8 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2S)-2-[4-(3-fluorophenyl)-3-hydroxybutyl]-5-oxo-1-pyrrolidinyl]propyl]-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



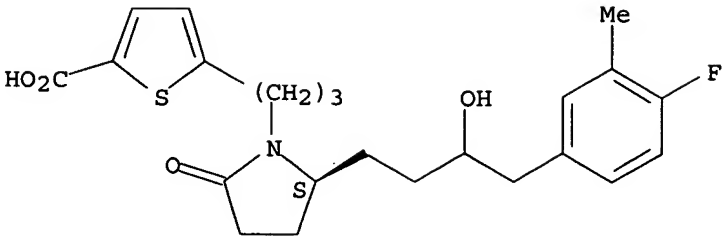
RN 431989-90-1 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2S)-2-[4-(4-ethylphenyl)-3-hydroxybutyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



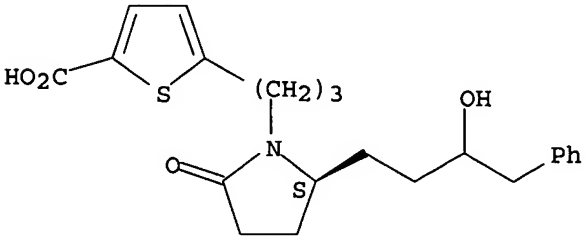
RN 431989-95-6 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2S)-2-[4-(4-fluoro-3-methylphenyl)-3-hydroxybutyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



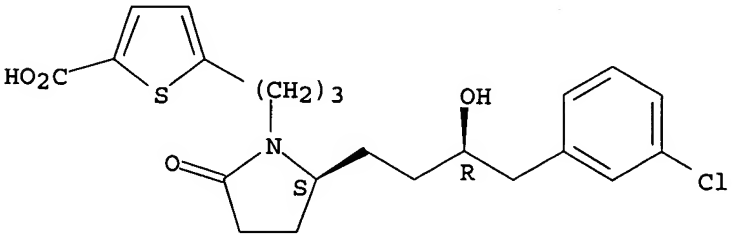
RN 431990-00-0 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2S)-2-(3-hydroxy-4-phenylbutyl)-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



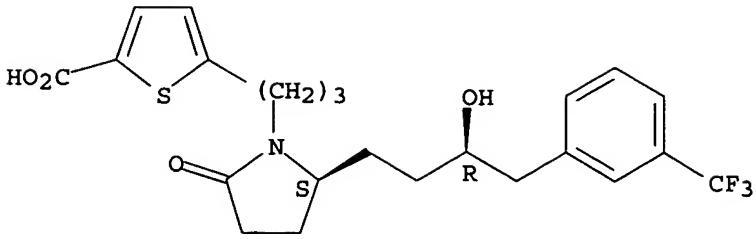
RN 431990-04-4 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2S)-2-[(3R)-4-(3-chlorophenyl)-3-hydroxybutyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



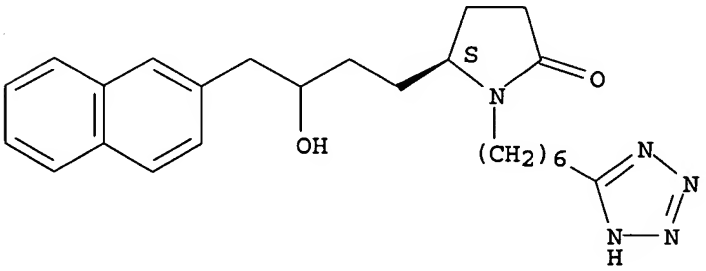
RN 431990-08-8 CAPLUS
CN 2-Thiophenecarboxylic acid, 5-[3-[(2S)-2-[(3R)-3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl]-5-oxo-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



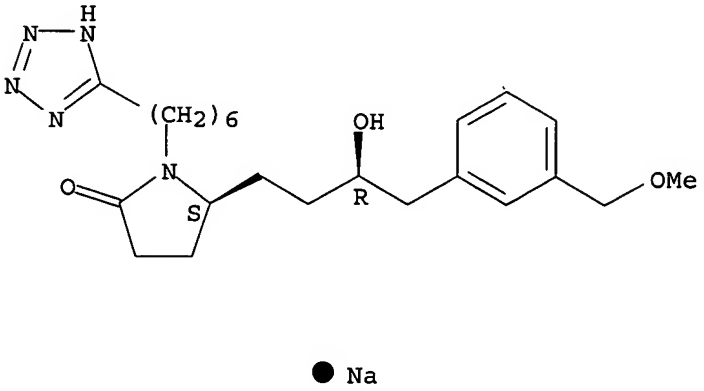
RN 431990-12-4 CAPLUS
CN 2-Pyrrolidinone, 5-[3-hydroxy-4-(2-naphthalenyl)butyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 431990-20-4 CAPLUS
CN 2-Pyrrolidinone, 5-[(3R)-3-hydroxy-4-[3-(methoxymethyl)phenyl]butyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, monosodium salt, (5S)- (9CI) (CA INDEX NAME)

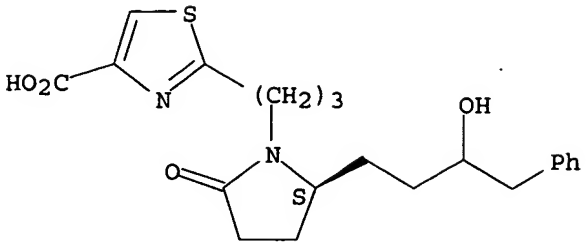
Absolute stereochemistry.



● Na

RN 431990-27-1 CAPLUS
CN 4-Thiazolecarboxylic acid, 2-[3-[(2S)-2-(3-hydroxy-4-phenylbutyl)-5-oxo-1-pyrrolidinyl]propyl]-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

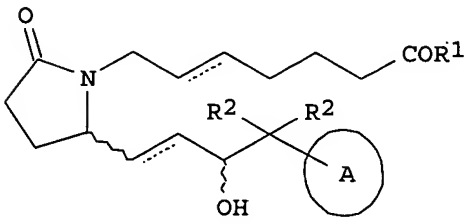


● Na

L9 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:240727 CAPLUS
DOCUMENT NUMBER: 136:279265
TITLE: EP4 receptor agonists containing 8-azaprostaglandin derivatives as active ingredients
INVENTOR(S): Maruyama, Tohru; Kobayashi, Kaoru; Maruyama, Takayuki
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002024647	A1	20020328	WO 2001-JP8176	20010920
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001090250	A5	20020402	AU 2001-90250	20010920
PRIORITY APPLN. INFO.:			JP 2000-286696 A	20000921
			WO 2001-JP8176 W	20010920

OTHER SOURCE(S): MARPAT 136:279265
GI



I

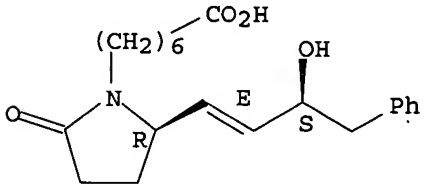
AB EP4 receptor agonists contain as the active ingredients 8-azaprostaglandin derivs. represented by the general formula I [R1 = OH, etc.; ring A = benzene ring, etc.; both R2 are H or F; the dotted line indicates a single or double bond; a proviso is given]. The compds. represented by the general formula I are useful as preventives and/or remedies for immune diseases, asthma, diseases in association with decrease in bone mass, pulmonary injury, pulmonary fibrosis, bronchitis, chronic obstructive respiratory diseases, hepatitis, nephritis, hypertension, myocardial ischemia, systemic inflammatory syndrome, sepsis, burn, systemic granuloma, ulcerative colitis, Crohn's disease, multiorgan failure, etc. In an in vitro test for EP4 agonist activity, ±(R,S)-7-(2-((1E)-3-hydroxy-4-phenyl-1-butenyl)-5-oxopyrrolidino)heptanoic acid showed an EC50 value of 0.5 μM. Formulations are given.

IT **66598-57-0 66598-64-9 66598-69-4**
66598-72-9 82303-00-2 82303-08-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(EP4 receptor agonists containing 8-azaprostaglandin derivs. as active ingredients)

RN 66598-57-0 CAPLUS

CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

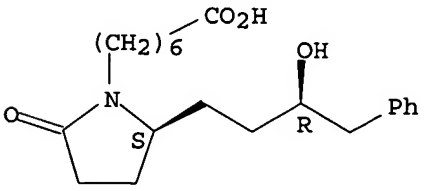
Absolute stereochemistry.
Double bond geometry as shown.



RN 66598-64-9 CAPLUS

CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-phenylbutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

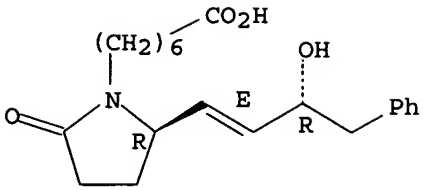
Absolute stereochemistry.



RN 66598-69-4 CAPLUS

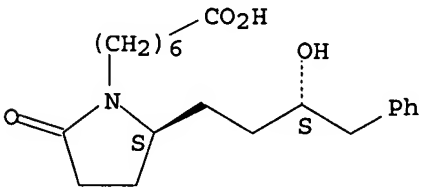
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3R)-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



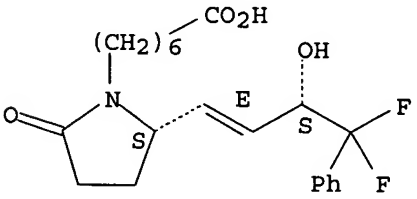
RN 66598-72-9 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3S)-3-hydroxy-4-phenylbutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



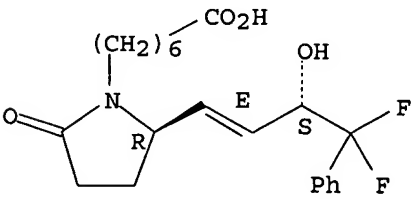
RN 82303-00-2 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



RN 82303-08-0 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



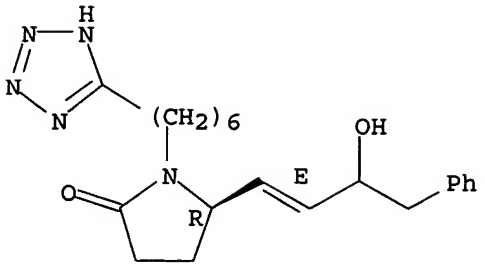
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:624143 CAPLUS
DOCUMENT NUMBER: 135:190414
TITLE: Use of EP4 receptor agonists for treatment of acute or chronic renal failure and drug compositions containing the agonists
INVENTOR(S): Paralkar, Vishwas Madhav; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001233792	A2	20010828	JP 2001-21534	20010130
EP 1132086	A2	20010912	EP 2001-300690	20010125
EP 1132086	A3	20020109		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2332687	AA	20010731	CA 2001-2332687	20010129
US 2001041729	A1	20011115	US 2001-771164	20010129
US 6610719	B2	20030826		
ZA 2001000827	A	20020730	ZA 2001-827	20010130
NZ 509632	A	20030131	NZ 2001-509632	20010130
AU 774569	B2	20040701	AU 2001-16722	20010130
PRIORITY APPLN. INFO.:			US 2000-178968P P	20000131

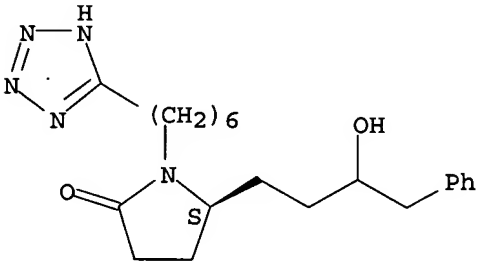
OTHER SOURCE(S): MARPAT 135:190414
AB Selective EP4 receptor agonists, their isomers, their prodrugs, or their salts are useful for treatment of acute or chronic renal failure or conditions caused from the renal failure in mammals. Drug compns. containing them are also claimed. A Markush structure as an example of the agonist is also given. 7-[2-(3-Hydroxy-4-phenylbutyl)-5-oxopyrrolidin-1-yl]-heptanoic acid significantly increased survival rate of acute renal failure model rats.
IT **356528-09-1 356528-10-4 356528-11-5 356528-12-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(EP4 receptor agonists for treatment of acute or chronic renal failure)
RN 356528-09-1 CAPLUS
CN 2-Pyrrolidinone, 5-[(1E)-3-hydroxy-4-phenyl-1-butenyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



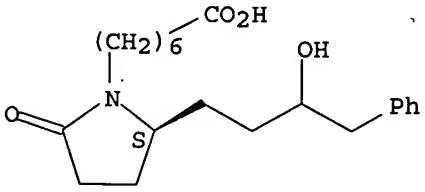
RN 356528-10-4 CAPLUS
CN 2-Pyrrolidinone, 5-(3-hydroxy-4-phenylbutyl)-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



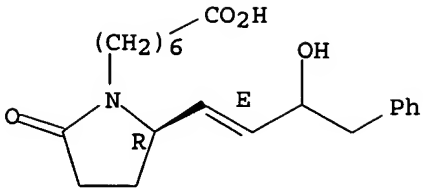
RN 356528-11-5 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-(3-hydroxy-4-phenylbutyl)-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 356528-12-6 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E)-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L9 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:581445 CAPLUS
DOCUMENT NUMBER: 135:147462
TITLE: Treatment of osteoporosis with EP2/EP4 receptor selective agonists
INVENTOR(S): Cameron, Kimberly O'Keefe; Thompson, David Duane; Lefker, Bruce Allen; Ke, Hua Zhu
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 29 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

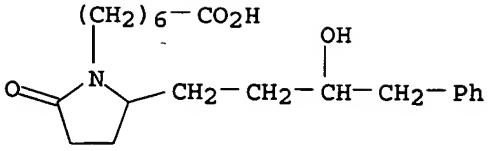
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1121939	A2	20010808	EP 2001-300999	20010205
EP 1121939	A3	20030910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001056060	A1	20011227	US 2001-776430	20010202
CA 2334257	AA	20010807	CA 2001-2334257	20010205
CA 2334257	C	20040817		
JP 2001220357	A2	20010814	JP 2001-30760	20010207
BR 2001000381	A	20011030	BR 2001-381	20010207
PRIORITY APPLN. INFO.:			US 2000-180635P P	20000207

OTHER SOURCE(S): MARPAT 135:147462

AB The invention provides methods and pharmaceutical compns. comprising prostaglandin agonists which are useful to prevent bone loss, restore or augment bone mass, and to enhance bone healing including the treatment of conditions which present with low bone mass, such as osteoporosis, and/or bone defects in vertebrates, and particularly mammals, including humans. The invention specifically provides methods and pharmaceutical compns. comprising combinations of EP2 receptor selective agonists and EP4 receptor selective agonists, as well as methods and pharmaceutical compns. comprising agents which are agonists for both the EP2 receptor and the EP4 receptor.

IT **352423-05-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(EP2/EP4 receptor selective agonists for treatment of osteoporosis)

RN 352423-05-3 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-(3-hydroxy-4-phenylbutyl)-5-oxo- (9CI) (CA INDEX NAME)



L9 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:472667 CAPLUS
DOCUMENT NUMBER: 135:76786
TITLE: Preparation of (tetrazolylhexyl)pyrrolidinones and oxopyrrolidineheptanoic acids as EP4 receptor selective agonists for the treatment of osteoporosis
INVENTOR(S): Cameron, Kimberly O'Keefe; Ke, Huazhu; Lefker, Bruce Allen; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001046140	A1	20010628	WO 2000-IB1711	20001120
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000016560	A	20020910	BR 2000-16560	20001120
TR 200201643	T2	20021121	TR 2002-200201643	20001120
EE 200200355	A	20031015	EE 2002-355	20001120
EP 1110949	A1	20010627	EP 2000-311034	20001211
EP 1110949	B1	20030924		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 250575	E	20031015	AT 2000-311034	20001211
PT 1110949	T	20031231	PT 2000-311034	20001211
ES 2204458	T3	20040501	ES 2000-311034	20001211
US 2001047105	A1	20011129	US 2000-738670	20001215
US 6737437	B2	20040518		
CA 2329678	AA	20010622	CA 2000-2329678	20001220
ZA 2000007694	A	20020620	ZA 2000-7694	20001220
AU 763983	B2	20030807	AU 2000-72393	20001220
JP 2001181210	A2	20010703	JP 2000-390594	20001222
US 2002040149	A1	20020404	US 2001-991585	20011116
US 6642266	B2	20031104		
NO 2002002925	A	20020618	NO 2002-2925	20020618
BG 106882	A	20030228	BG 2002-106882	20020628

PRIORITY APPLN. INFO.:
US 1999-171353P P 19991222
WO 2000-IB1711 W 20001120
US 2000-738670 A3 20001215

OTHER SOURCE(S): MARPAT 135:76786
GI

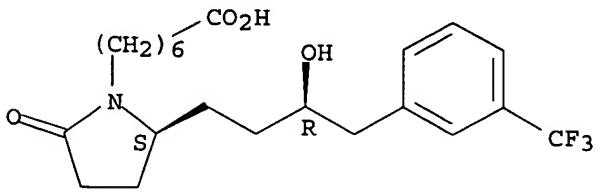
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB This invention is directed to methods of treating conditions that present with low bone mass, particularly osteoporosis, frailty, an osteoporotic fracture, a bone defect, childhood idiopathic bone loss, alveolar bone loss, mandibular bone loss, bone fracture, osteotomy, bone loss associated with periodontitis, or prosthetic ingrowth comprising administering prostaglandin agonists which are EP4 receptor selective prostaglandin agonists. The invention is especially directed to methods wherein the EP4 receptor selective agonists are pyrrolidinones I [Q = CO2R3, CONHR4, tetrazol-5-yl; A, B = CH2CH2, cis-CH:CH; X = (R)- H,OH; (S)- H, OH; H, OH; R2 = 2-thienyl, Ph, PhO, chloro-, fluoro, Ph, methoxy, trifluoromethyl-, or alkyl-substituted Ph and PhO; R3 = H, alkyl, Ph, p-biphenylyl; R4 = COR5, SO2R5; R5 = Ph, alkyl] and their prodrugs and pharmaceutically acceptable salts which were prepared Thus, condensation of 3-ClC6H4CH2COCH2P(O)(OMe)2 with the formylpyrrolidineheptanoate II in THF containing NaH gave the (oxobutenyl)pyrrolidineheptanoate III. III underwent successive stereoselective reduction using a chiral oxazaborolidine, hydrogenation, and saponification to give the [(chlorophenyl)hydroxybutyl]pyrrolid ineheptanoate IV.

IT **346672-61-5P 346672-71-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of EP4 receptor prostaglandin agonist (oxopyrrolidine)heptanoates and tetrazolylhexylpyrrolidinones for treatment of osteoporosis)

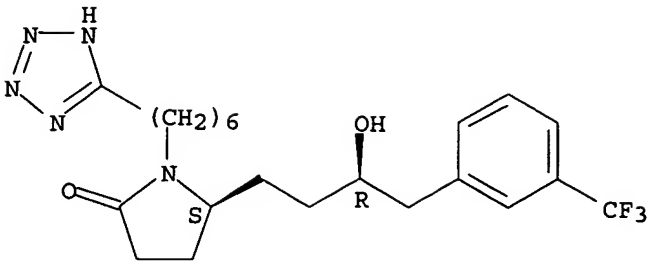
RN 346672-61-5 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 346672-71-7 CAPLUS
CN 2-Pyrrolidinone, 5-[(3R)-3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

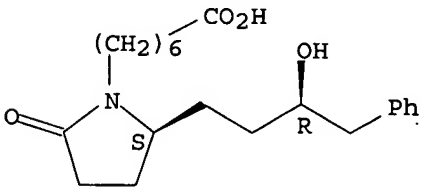
Absolute stereochemistry.



IT **66598-64-9P 346672-57-9P 346672-62-6P**
346672-67-1P 346672-72-8P 346672-76-2P
346672-80-8P 346672-84-2P 346672-87-5P
346672-93-3P 346673-06-1P 346673-07-2P
346673-08-3P 346673-09-4P 346673-10-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of EP4 receptor prostaglandin agonist (oxopyrrolidine)heptanoates and tetrazolylhexylpyrrolidinones for treatment of osteoporosis)

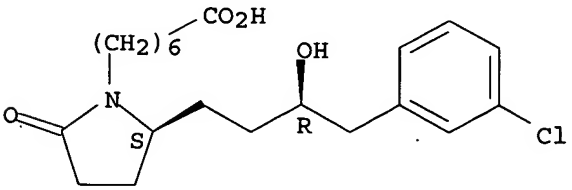
RN 66598-64-9 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-phenylbutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



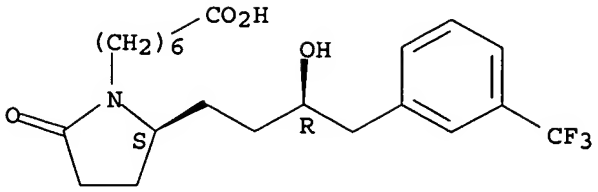
RN 346672-57-9 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-4-(3-chlorophenyl)-3-hydroxybutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 346672-62-6 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl]-5-oxo-, monosodium salt, (2S)- (9CI) (CA INDEX NAME)

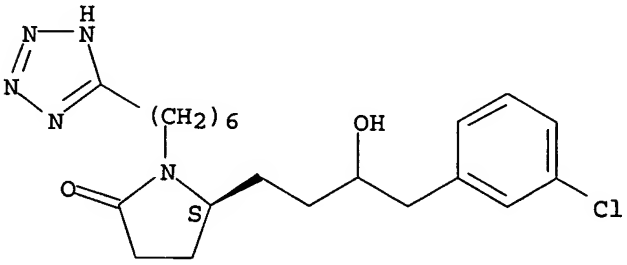
Absolute stereochemistry.



● Na

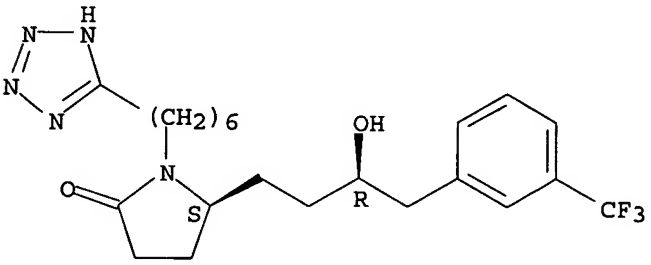
RN 346672-67-1 CAPLUS
CN 2-Pyrrolidinone, 5-[4-(3-chlorophenyl)-3-hydroxybutyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



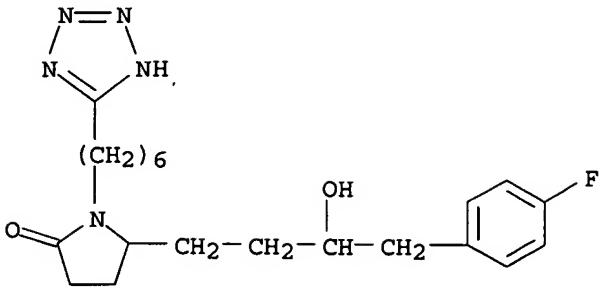
RN 346672-72-8 CAPLUS
CN 2-Pyrrolidinone, 5-[(3R)-3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, monosodium salt, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

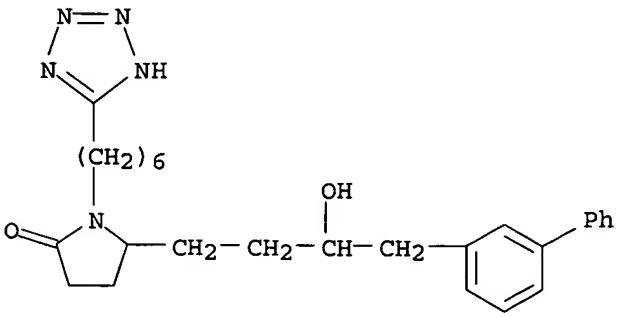


● Na

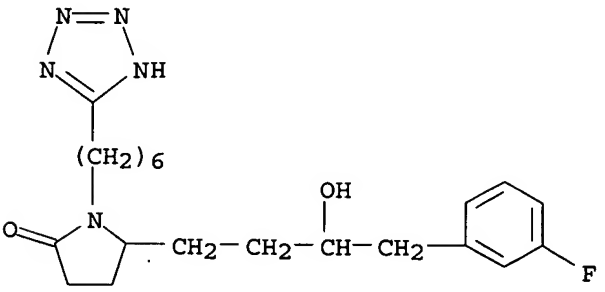
RN 346672-76-2 CAPLUS
CN 2-Pyrrolidinone, 5-[4-(4-fluorophenyl)-3-hydroxybutyl]-1-[6-(1H-tetrazol-5-yl)hexyl]- (9CI) (CA INDEX NAME)



RN 346672-80-8 CAPLUS
CN 2-Pyrrolidinone, 5-(4-[1,1'-biphenyl]-3-yl-3-hydroxybutyl)-1-[6-(1H-tetrazol-5-yl)hexyl]- (9CI) (CA INDEX NAME)

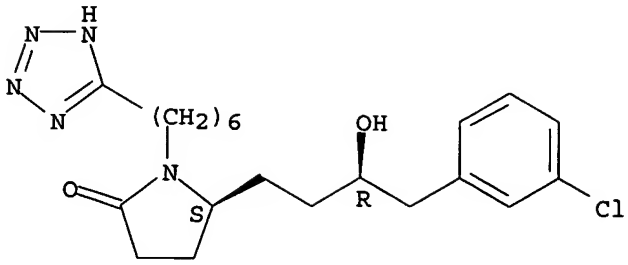


RN 346672-84-2 CAPLUS
CN 2-Pyrrolidinone, 5-[4-(3-fluorophenyl)-3-hydroxybutyl]-1-[6-(1H-tetrazol-5-yl)hexyl]- (9CI) (CA INDEX NAME)



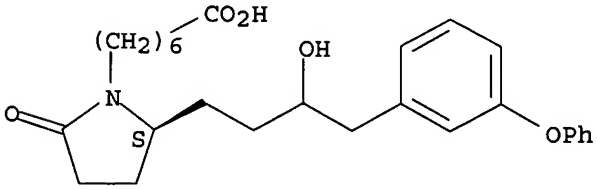
RN 346672-87-5 CAPLUS
CN 2-Pyrrolidinone, 5-[(3R)-4-(3-chlorophenyl)-3-hydroxybutyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



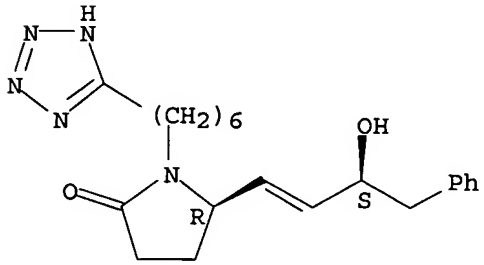
RN 346672-93-3 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[3-hydroxy-4-(3-phenoxyphenyl)butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



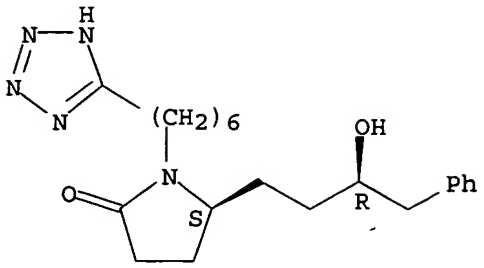
RN 346673-06-1 CAPLUS
CN 2-Pyrrolidinone, 5-[(3S)-3-hydroxy-4-phenyl-1-butenyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



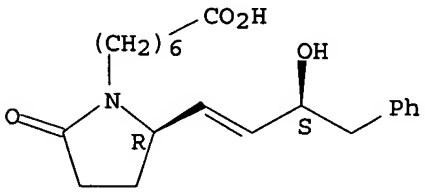
RN 346673-07-2 CAPLUS
CN 2-Pyrrolidinone, 5-[(3R)-3-hydroxy-4-phenylbutyl]-1-[6-(1H-tetrazol-5-yl)hexyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



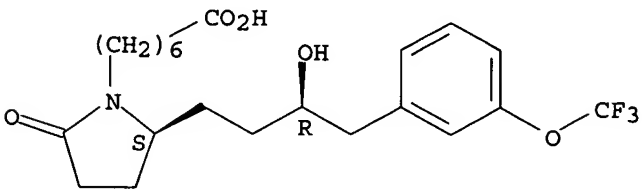
RN 346673-08-3 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3S)-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



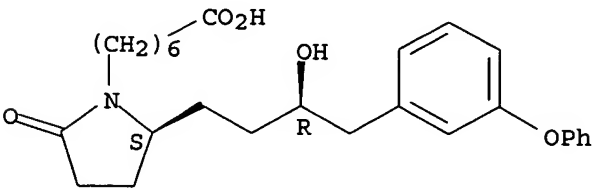
RN 346673-09-4 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-[3-(trifluoromethoxy)phenyl]butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 346673-10-7 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-(3-phenoxyphenyl)butyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



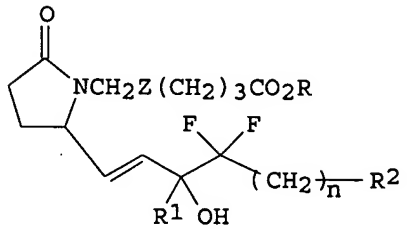
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:438745 CAPLUS
DOCUMENT NUMBER: 97:38745
TITLE: 8-Aza-16,16-difluoroprostanoids
INVENTOR(S): Scribner, Richard Merrill
PATENT ASSIGNEE(S): du Pont de Nemours, E. I., and Co., USA
SOURCE: Eur. Pat. Appl., 64 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 46082	A2	19820217	EP 1981-303641	19810810
EP 46082	A3	19820303		
EP 46082	B1	19850605		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4320136	A	19820316	US 1980-176784	19800811
CA 1161447	A1	19840131	CA 1981-383299	19810806
DK 8103522	A	19820212	DK 1981-3522	19810807
JP 57054166	A2	19820331	JP 1981-124205	19810810
AT 13667	E	19850615	AT 1981-303641	19810810

PRIORITY APPLN. INFO.: US 1980-176784 A 19800811
EP 1981-303641 A 19810810
OTHER SOURCE(S): CASREACT 97:38745
GI



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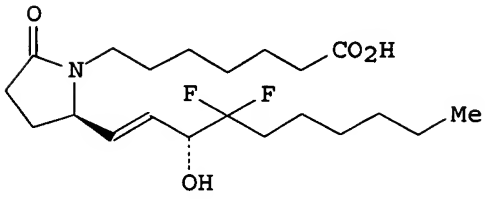
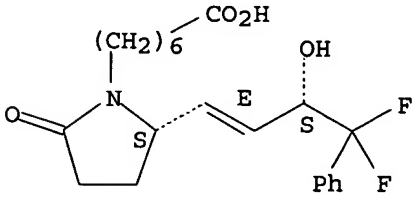


II

AB Racemic and optically active I [Z = CH2CH2, CH:CH, C.tplbond.C; R = H, C1-12 alkyl, cycloalkyl; R1 = H, Me, Et; R2 = Me, CF3, (un)substituted phenyl; n = 0-2 if R2 = aryl and 3-8 if R2 = Me or CF3] and their salts were prepared by appropriate modification of conventional methods. Typical of compds. prepared was II, whose Me ester gave better short-term gastric protection than PGE1 and at 5 mg/kg gave 80% protection against histamine-induced bronchoconstriction at 2 h orally.

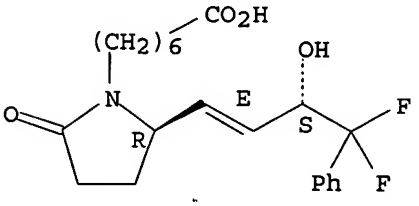
IT **82303-00-2P 82303-08-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 82303-00-2 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



RN 82303-08-0 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3R)-4,4-difluoro-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



L9 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1980:146340 CAPLUS
DOCUMENT NUMBER: 92:146340
TITLE: 1,5-Disubstituted-2-pyrrolidones
INVENTOR(S): Nelson, Albin J.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 19 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

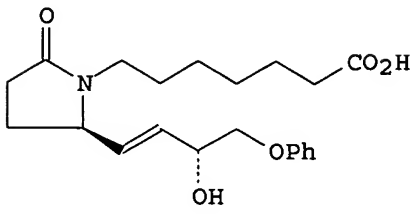
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4177346	A	19791204	US 1978-885908	19780313
SE 7708642	A	19780207	SE 1977-8642	19770727
SE 423813	B	19820607		
SE 423813	C	19820916		
CA 1077948	A1	19800520	CA 1977-283598	19770727
IL 52615	A1	19810913	IL 1977-52615	19770728
AU 7727515	A1	19790208	AU 1977-27515	19770801
AU 508007	B2	19800306		
NL 7708637	A	19780208	NL 1977-8637	19770804

ZA 7704704	A	19780628	ZA 1977-4704	19770804
BE 857506	A1	19780206	BE 1977-8318	19770805
DK 7703520	A	19780207	DK 1977-3520	19770805
FI 7702376	A	19780207	FI 1977-2376	19770805
FI 70009	B	19860131		
FI 70009	C	19860912		
NO 7702752	A	19780207	NO 1977-2752	19770805
FR 2369260	A1	19780526	FR 1977-24290	19770805
FR 2369260	B1	19820212		
ES 461388	A1	19781201	ES 1977-461388	19770805
DD 136135	C	19790620	DD 1977-200468	19770805
GB 1556569	A	19791128	GB 1977-33002	19770805
GB 1556570	A	19791128	GB 1978-43588	19770805
SU 703016	D	19791205	SU 1977-2511155	19770805
DD 143768	C	19800910	DD 1977-213369	19770805
CH 624934	A	19810831	CH 1977-9646	19770805
HU 22714	O	19820628	HU 1977-PI587	19770805
HU 180273	B	19830228		
CS 221269	P	19830429	CS 1977-5202	19770805
JP 53021159	A2	19780227	JP 1977-94589	19770806
JP 55031147	B4	19800815		
AT 7705794	A	19801115	AT 1977-5794	19770808
AT 362887	B	19810625		
PL 112931	B1	19801129	PL 1977-215666	19770808
RO 72530	P	19820201	RO 1977-91464	19770826
ES 471349	A1	19790916	ES 1978-471349	19780701
SU 818480	A3	19810330	SU 1978-2672200	19781011
SU 850000	A3	19810723	SU 1978-2674602	19781017
JP 55055161	A2	19800422	JP 1979-112743	19790903
JP 58005196	B4	19830129		
CA 1084939	A2	19800902	CA 1980-343178	19800107
DK 8004725	A	19801107	DK 1980-4725	19801107
DK 146179	B	19830718		
DK 146179	C	19831212		

PRIORITY APPLN. INFO.:

US 1976-712362	A2	19760806
CA 1977-283598	A3	19770727
DK 1977-3520	A	19770805

GI



I

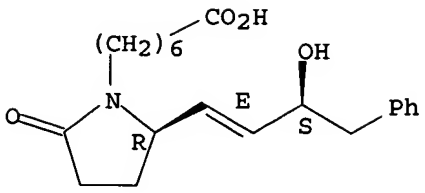
AB A series of known 8-azaprostaglandins (e.g., I) was prepared conventionally.

IT **66598-57-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and protection with dihydropyran)

RN 66598-57-0 CAPLUS

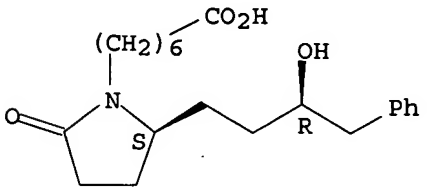
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **66598-64-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 66598-64-9 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-phenylbutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1978:405993 CAPLUS
DOCUMENT NUMBER: 89:5993
TITLE: 1,5-Disubstituted 2-pyrrolidones
INVENTOR(S): Nelson, Albin James
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Ger. Offen., 82 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2735904	A1	19780209	DE 1977-2735904	19770805
SE 7708642	A	19780207	SE 1977-8642	19770727
SE 423813	B	19820607		
SE 423813	C	19820916		
CA 1077948	A1	19800520	CA 1977-283598	19770727
IL 52615	A1	19810913	IL 1977-52615	19770728
AU 7727515	A1	19790208	AU 1977-27515	19770801
AU 508007	B2	19800306		
NL 7708637	A	19780208	NL 1977-8637	19770804
ZA 7704704	A	19780628	ZA 1977-4704	19770804
BE 857506	A1	19780206	BE 1977-8318	19770805
DK 7703520	A	19780207	DK 1977-3520	19770805
FI 7702376	A	19780207	FI 1977-2376	19770805
FI 70009	B	19860131		
FI 70009	C	19860912		
NO 7702752	A	19780207	NO 1977-2752	19770805

FR 2369260	A1	19780526	FR 1977-24290	19770805
FR 2369260	B1	19820212		
ES 461388	A1	19781201	ES 1977-461388	19770805
DD 136135	C	19790620	DD 1977-200468	19770805
GB 1556569	A	19791128	GB 1977-33002	19770805
GB 1556570	A	19791128	GB 1978-43588	19770805
SU 703016	D	19791205	SU 1977-2511155	19770805
DD 143768	C	19800910	DD 1977-213369	19770805
CH 624934	A	19810831	CH 1977-9646	19770805
HU 22714	O	19820628	HU 1977-PI587	19770805
HU 180273	B	19830228		
CS 221269	P	19830429	CS 1977-5202	19770805
JP 53021159	A2	19780227	JP 1977-94589	19770806
JP 55031147	B4	19800815		
AT 7705794	A	19801115	AT 1977-5794	19770808
AT 362887	B	19810625		
PL 112931	B1	19801129	PL 1977-215666	19770808
RO 72530	P	19820201	RO 1977-91464	19770826
ES 471349	A1	19790916	ES 1978-471349	19780701
SU 818480	A3	19810330	SU 1978-2672200	19781011
SU 850000	A3	19810723	SU 1978-2674602	19781017
JP 55055161	A2	19800422	JP 1979-112743	19790903
JP 58005196	B4	19830129		
CA 1084939	A2	19800902	CA 1980-343178	19800107
DK 8004725	A	19801107	DK 1980-4725	19801107
DK 146179	B	19830718		
DK 146179	C	19831212		

PRIORITY APPLN. INFO.:

US 1976-712362	A	19760806
CA 1977-283598	A3	19770727
DK 1977-3520	A	19770805

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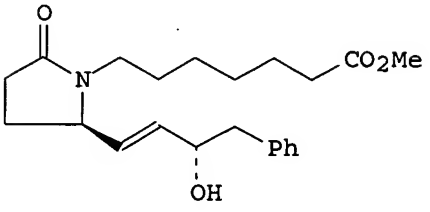

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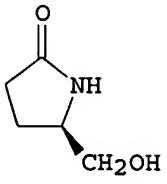


II

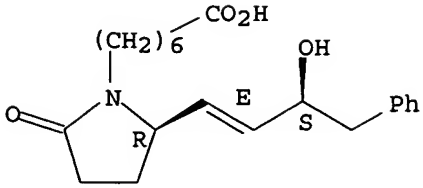
AB A series of 29 8-azaprostaglandins and intermediates for them, e.g. I, was prepared from (+)-II by, e.g., protecting with dihydropyran, alkylating with, e.g., Br(CH2)6CO2Et, deprotecting, oxidizing the CH2OH group to the aldehyde, condensing with the appropriate phosphorus ylide, and reducing with borohydride.

IT **66598-57-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and protection with dihydropyran)

RN 66598-57-0 CAPLUS

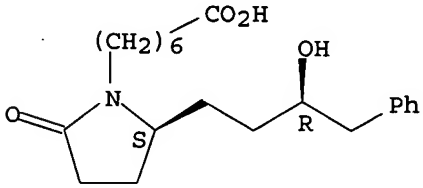
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3S)-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



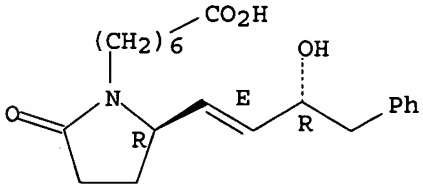
IT **66598-64-9P 66598-69-4P 66598-72-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 66598-64-9 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3R)-3-hydroxy-4-phenylbutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



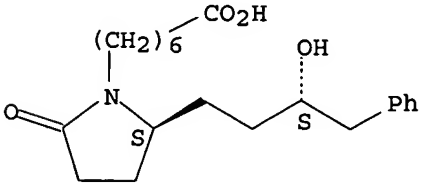
RN 66598-69-4 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(1E,3R)-3-hydroxy-4-phenyl-1-butenyl]-5-oxo-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 66598-72-9 CAPLUS
CN 1-Pyrrolidineheptanoic acid, 2-[(3S)-3-hydroxy-4-phenylbutyl]-5-oxo-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	106.98	438.82

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-15.33	-16.06

STN INTERNATIONAL LOGOFF AT 10:59:18 ON 25 JAN 2005